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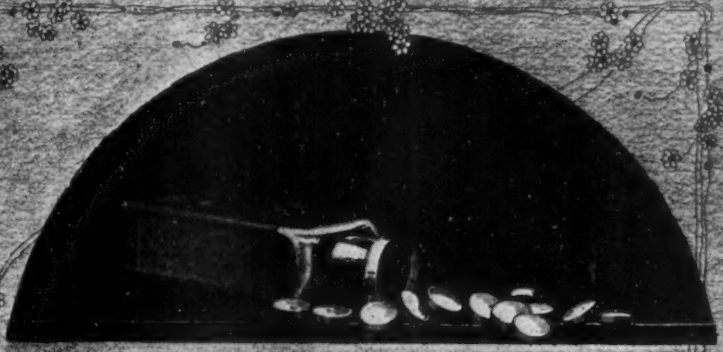

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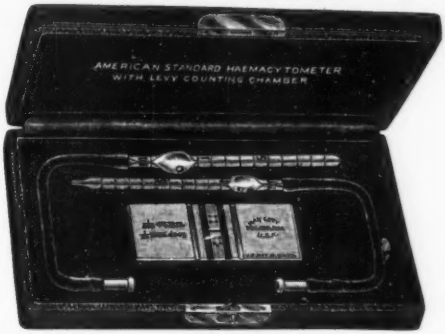

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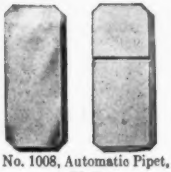

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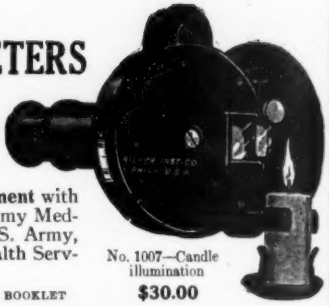

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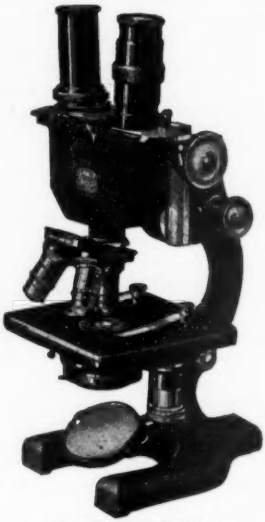

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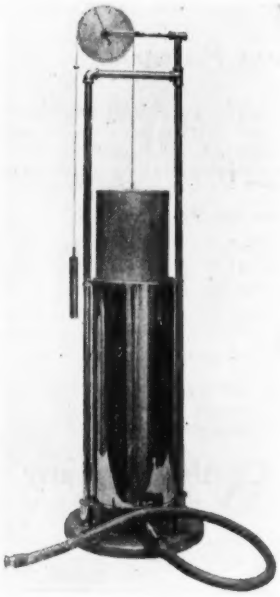

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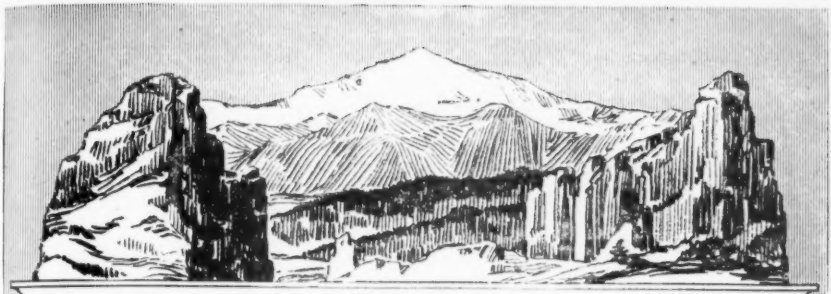

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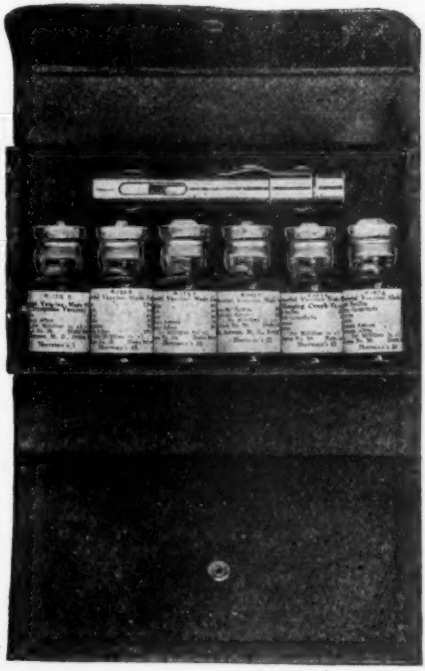

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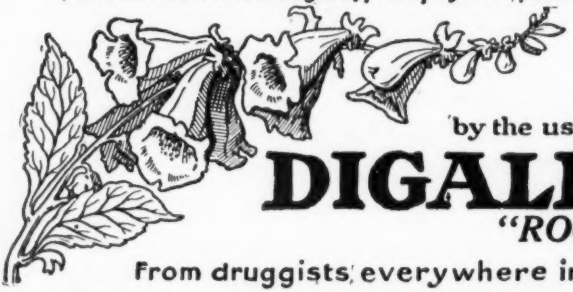

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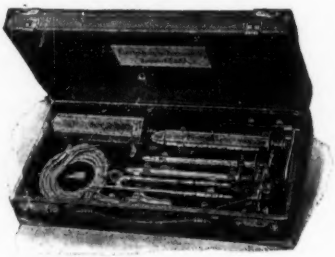

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MARCH, 1921

ORIGINAL ARTICLES.

THE IMPORTANCE OF RECOGNIZING AND TREATING NEUROSYPHILIS IN THE EARLY PERIOD OF THE INFECTION.

By John A. Fordyce, M.D.,

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A comprehensive grasp of the syphilis problem cannot be obtained by the study of one phase only of the disease. A degenerated brain or a tract sclerosis studied by the neuropathologist visualizes the end-result of the treponema infection. It does not reveal the early beginnings of the disease nor indicate the therapeutic measures which might have prevented the terminal stage. The sudden onset of cerebral or spinal symptoms should not necessarily be interpreted as the result of an immediate invasion of the nervous system but rather as a tissue reaction of slowly progressive character. A close analogy is afforded by the study of the aortic changes in aneurysm as related to the early involvement of the adventitial vessels. The same arguments may be employed in the study of the visceral and other lesions in syphilis and conclusions deduced that degenerative changes are of slow progress and often require years before functional impairment is manifest. We must furthermore recognize the fact that the fundamental reactive phenomena are the same in the initial lesion which ushers in the infection and the vessel changes in paresis which end the luetic tragedy.

It seems needless to emphasize the importance of the study of syphilis as a general infection and the necessity of correlating the

observations of all medical workers who have to do with it. Various specialists observe the local lesions in the eye, throat, skin and other organs, and can often control them by short courses of treatment. These manifestations are the accidents or episodes of a general infection. The cure of visible lesions does not mean the cure of the underlying disease. It progresses in a modified manner in other tissues which are not seen and is then known as latent asymptomatic syphilis, an unfortunate expression which deceives the patient as well as his medical adviser. Syphilis of the nervous system should be restudied from both the clinical and serologic standpoint and the significance of the earlier infection emphasized in its bearing on the later degenerations. The highly specialized character of medical practice does not permit any one observer to see more than a few phases of the disease. Close and sympathetic coöperation between workers in many specialities can better advance our general knowledge. Institutions which contain individual groups, each willing to learn from the other, offer the best opportunities for mutual advance. In the past the dermatologist has emphasized chiefly the external evidences of the disease and has neglected in great measure the widely disseminated infection. Fortunately this criticism is no longer valid, as many observers are now engaged on the problem of the general disease in its relations to future changes in the nervous system and viscera.

The infectious agent in syphilis in its relation to the defensive forces of the body is analogous to other protozoan organisms. It may be modified, but is seldom controlled, by antibody or other immunity processes. Tissues may harbor the treponemata for an indefinite time with little or no evidence of their presence. It has been demonstrated time and again that the nervous system may be the habitat of the organisms, with little or no tissue reaction, until a traumatism or some exciting factor stimulates their activity, or until sufficient time has elapsed to permit centers or tracts to be compromised which give rise to objective signs or symptoms.

As a routine method of examination and control, spinal fluid examinations are made by few physicians in early syphilis. From this neglect many cases are overlooked because of their asymptomatic character. As time progresses these asymptomatic cases may develop vague mental or physical symptoms which are frequently wrongly interpreted by their physician until definite focal signs make their appearance. At this time neurosyphilis is said to exist, but little or no attempt is made to correlate the end-result of the infection with the indefinite signs and symptoms which have preceded. The failure of therapeutic methods to cure the terminal results of an infection leads to pessimistic views as to the utility in any stage and permits the diffusion of a large amount of false and misleading information.

Physiologic knowledge leading to the employment of exact

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methods in diagnosing well-established focal lesions and tract degenerations has reached a high degree of perfection. It affords the physician much gratification to accurately determine the site of pathologic changes. The patient at this stage of his disease is an interesting study in brain or cord localization. The activity of a syphilitic process in the central nervous system is, however, indicated much earlier, more accurately and often only by the cytologic changes in the spinal fluid which should always supplement the physical examination. No matter what views we may hold as to the physiology or origin of the fluid the activity of syphilis of the central nervous system is usually reflected in the well-known phases of Nonne and the gold sol reaction long before mental or physical signs are present. Failure to utilize this important method of investigation in early syphilis leads inevitably to many unrecognized and slowly progressive types of neurosyphilis. Neglect of systematic eye-ground examinations in the active stage of the disease will likewise cause many cases of beginning optic neuritis to be overlooked.

Why should one await advanced degeneration in important organs and stand helpless in their presence when their early beginnings may be detected? The fate of a syphilitic individual as regards his future immunity to neurosyphilis rests largely on the result of a spinal fluid examination, either during his treatment or before his final discharge, and if infection is present, on its complete clinical and serologic cure. Both the patient and the physician are too often satisfied with a symptomatic cure and a disappearance of the obtrusive signs.

A prolonged study of early cases of neurosyphilis as regards the therapeutic response of the fluid changes to treatment has convinced me that on the one hand we have superficial types rapidly curable and on the other deeper ones which yield only to prolonged treatment. In their therapeutic response and fluid formula the latter are probably of the preparetic type which without treatment would eventually result in degenerative encephalitis.

By piecing together scattered observations supplemented by a certain amount of scientific imagination a mosaic can be constructed which conveys a picture of this far-reaching disease. The long experience, careful observations and keen clinical insight of Alfred Fournier, who saw all phases of syphilis, enabled him to interpret its relationship to tabes, paresis and other affections of the central nervous system which he designated "parasyphilis." Had he then been able to supplement his clinical observations with the modern discoveries of the Treponema pallidum, complement-fixation reaction and the cytobiology of the spinal fluid the necessity for devising the term "parasyphilis" would not have existed.

As the result of animal experimentation we can now follow the treponema from its first implantation and note the reactive phe-

nomena which attend its deposition in the tissues. Likewise clinical and pathologic studies in human syphilis afford good reasons and some direct observations which make it probable that foci are established in the various organs during the early florid stage of the disease. These foci may slowly cause tissue changes or the organs may harbor the treponema without reactions for an indefinite time. In numerous publications I have presented certain arguments based on observations and study of the general pathology of the disease which have convinced me that practically all types of neurosyphilis originate within the first year of the infection, and are then amenable to properly applied therapeusis. The results following the practical application of this working hypothesis have fully justified its adoption.

The experimental work of Nichols, Reasoner and others, supported by the clinical observations of many investigators as to the existence of familial types of neurosyphilis, afford strong arguments in favor of a strain of the treponema with neurotropic affinities or rapid invasive power. The absence of skin manifestations in a large percentage of cases of syphilis of the nervous system further distinguishes this strain from the usual one. Because of its greater invasive power or its attraction to nerve tissues it implicates these structures early in the infection in about 25 per cent. of all cases of syphilis. The number of cases revealed by fluid examination in the early period of the disease corresponds roughly with the total number of cases of late neurosyphilis. We are obliged, therefore, to conclude that either the cases of early syphilis of the nervous system are cured, and that another and later invasion occurs, or that the early infection persists in the majority of cases uninfluenced by the usual therapeutic procedures.

Our clinical and serologic study of syphilis during the past ten years has definitely shown us that in the great majority of cases syphilis of the nervous system is not cured by the use of specific remedies employed in the usual way. Many symptoms disappear, the blood Wassermann becomes negative and the patient enjoys for a time a feeling of false security, only later to awaken to a knowledge of his real condition. For instance the case of Dr. A., who acquired a digital chancre in March, 1913, while performing an abdominal operation. In April he presented a macular rash and complained of severe pain along the vertebral column, which rendered motion almost impossible. He received sixteen injections of arsphenamin and two courses of mercury. The Wassermann was repeatedly negative. In January, 1918, he had a fainting attack. The Wassermann at this time being reported 2+ he took seven more injections of arsphenamin and a course of mercurial injections. The reaction again became negative. Another fainting attack occurred in April, 1920. Pains in the shoulders and over the chest had also been present for several weeks. Neurologic

examination showed only the slightest difference in the deep reflexes on the two sides and the right pupil a trifle larger than the left and a little more active. His blood-pressure was 140/108. Lumbar puncture revealed 195 cells; globulin, 4+; Wassermann, 4+ to 0.1 c.c.; gold sol luetic curve. The blood was negative with cholesterinized antigen and 2+ with alcoholic antigen (ice-box fixation).

Another case is F., aged thirty years, who was treated intensively during the early secondary period of his infection, which occurred in May, 1912. At first he was given neoarsphenamin, 1.2 gms. every other day for three doses; then three more same dosage at six-day intervals, followed by three injections of 0.75 gms. at weekly intervals and five injections of arsphenamin of 0.4 gms. In addition he had thirty-two injections of mercury salicylate, grains $1\frac{1}{2}$ to grains $2\frac{1}{2}$. The Wassermann was persistently negative and remained so after a provocative injection three years after infection. Consent to a lumbar puncture was not obtained. Recently he returned for another blood test and complained of vague pains in his arms and legs. The blood with all methods was 4+. His deep reflexes were more active on the right than on the left side. There were no pupillary changes or other physical findings. Spinal fluid revealed: Cells, 55; globulin, 3+; Wassermann, 4+ with 0.6 c.c.; gold sol luetic curve.

Observations of a similar kind several years ago caused us to modify our criteria of cure and to insist on a spinal fluid examination before final pronouncement. If the spinal fluid is negative in all its phases after the other criteria of cure are complied with we can assure our patient, with a considerable degree of confidence, that he need have no fear of late neurosyphilis. In other words it is strongly probable the treponema invades the nervous system during the period of general dissemination or not at all.

One can readily see without a great tax on the imagination what enormous significance the general adoption of such examinations leading to proper diagnosis and treatment must have on the individual and what great economic importance it will have for society and the state. The question will doubtless be asked as to the reasons for the belief that infection of the nervous system does not occur later than in the early florid stage. We have not yet sufficient data to deny absolutely its possibility, but the arguments previously brought forward would seem to show that, as a usual method of infection of the central nervous system, in the light of our present knowledge of the cytobiology of the fluid it is extremely improbable.

In order to make scientific progress it is necessary, in the absence of exact knowledge, to adopt a plausible working theory based on known facts. If disproved by further observations it should be modified or discarded for one which more accurately accords with them. The theory in question is one which accords with many known facts. Properly employed therapeutic procedures controlled

by examinations of the spinal fluid cure practically all cases of early neurosyphilis. In none of the cases cured serologically and clinically have we seen later active recurrences. If subsequent experience confirms these results we may safely assume that it is possible to eradicate absolutely the most feared of all the results of the disease.

The alternative procedure to the method I have outlined is the one usually followed, *i. e.*, treatment with arsphenamin and mercury for one or two years. After a negative Wassermann in the blood has continued for a definite time the patient is told the cure is complete. He returns within a few years or sooner with pupillary changes, modifications in his deep reflexes and other indications of nervous system involvement. If he is fortunate enough to fall in the hands of a practitioner who realizes the significance of the signs in question, and believes in the revelations of spinal fluid examinations, he may yet be amenable to prolonged treatment. As a rule these cases are overlooked or a wrong interpretation is placed on their signs or symptoms. Their disease progresses to the terminal degenerative stage.

The old view that the organism of syphilis may disseminate and invade the central nervous system at any time has nothing to support it except vague clinical impressions. It could only be determined by spinal fluid examination showing absence of early infection and by similar examination in the late stages proving the existence of it. No such proof exists, while all the evidence supports the contrary view. We have everything to gain and nothing to lose by adopting the hypothesis in question. We have everything to lose and nothing to gain by adherence to the older view.

It will require many years before practitioners of medicine fully realize the relationship of early involvement of the nervous system to the later degenerative stages of paresis and tabes and the importance of controlling the final cure by systematic fluid examinations. It will require a longer time before these early infections are systematically and properly treated. Until our public clinics are provided with proper facilities for diagnosis and treatment such cases will go unrecognized and neurosyphilis will continue to cut short the lives of many otherwise useful citizens. The need of better methods in treating syphilis of the central nervous system is felt by everyone who comes in contact with large numbers of syphilitic patients in all stages of the disease. The average treatment of syphilis even now with our recently acquired knowledge and new remedies is too often imperfectly carried out. A patient is discharged as cured after a definite amount of treatment regardless of the Wassermann reaction. Or, imperfectly interpreted by the practitioner, the patient is given a feeling of false security because his blood remains persistently negative and the spinal fluid is ignored, although a persistent infection of the nervous system is present with few or no obtrusive symptoms.

One should approach the therapeutic problem in neurosyphilis with an open mind without prejudice and uninfluenced by theories. Clinical and serologic cures are of vastly more value to the patient and to the progress of medicine than *a priori* arguments based on so-called physiologic reasons why they are not possible. None of our present methods of treatment are effective in all cases. Some are cured by intravenous methods alone or combined with mercury. When these methods fail spinal drainage may increase the permeability of the capillaries and lead to a greater penetration of the arsenic. The advocates of the drainage method unfortunately fail to furnish any proof of change in the various phases in the spinal fluid and speak in the most general terms of improvement. It is the old story of clinical impressions and vague statements of great change in the patient's condition without careful and prolonged clinical and laboratory control. I have had the opportunity to examine and treat a number of cases previously subjected to spinal drainage combined with intravenous treatment. In the majority, aside from minor changes in the cytology of the fluid, no improvement was observed. Intraspinal treatment in several of these cases has been followed by negative findings in the fluid and by clinical cures. It cannot justly be stated, therefore, that cures by intraspinal treatment are due to the incidental drainage. I have no brief to offer in behalf of an exclusive method of treatment, and only contend that after failure by the intravenous route we have a valuable procedure in the intraspinal method when used with the proper technic and where indications are present for it.

Condemnation of the method because it fails to cure deep-seated encephalitis and the degenerative stage of tabes is illogical and apart from the thesis I am endeavoring to uphold. My plea is for the use of exact methods in diagnosis which may reveal the early curative stages of neurosyphilis and for proper therapeutic procedures which may then be effective. If physiologic reasons oppose the employment of intraspinal therapy in syphilis of the nervous system they should likewise contra-indicate the use of antimeningitis serum in infectious cerebrospinal meningitis. As curative results are obtained in both conditions, might it not be safe to assume that a revision of the physiologic arguments may be necessary?

Intraspinal therapy is a safe procedure providing the proper technic is employed and judgment exercised in the selection of suitable cases. It is less dangerous than the intensive intravenous method following which severe jaundice, dermatitis or other ill-effects may be seen every day in a large clinic or private practice.

Intraspinal therapy is indicated in all early cases of neurosyphilis, such as meningitis, meningo-encephalitis or meningomyelitis which are not responding to the ordinary forms of treatment. It is contra-indicated, therefore, where there is clinical and serologic response to the intravenous mode of administration and in all cases with nega-

tive findings in the fluid even though clinical symptoms may be present.

In order to minimize the after-effects of intraspinal therapy patients should remain in bed for at least twenty-four hours, preferably forty-eight, and should not be permitted to get up for any reason whatever. Reactions are due (1) to the withdrawal of the fluid and may come on within a few hours in the form of headache —frontal, occipital or generalized—sometimes accompanied by vomiting; or the symptoms may be delayed until the patient is up and about for an hour or more, when headache or pain in the back of the neck or between the shoulders may supervene. These disappear on the resumption of the recumbent position. Patients with lumbar puncture headache should be kept in bed for several days, otherwise the headache may persist for two weeks or more. (2) As the result of treatment patients may complain of pains in the legs, sometimes of the back. They vary in severity from slight, transient pains to severe lightning-like pains. They are seldom met with in early cases but occur more frequently in tabetics, and require the use of opiates during the night, usually passing off the next day, although they may persist for several days. They should be taken as a guide to regulate the dosage and the interval: in patients who are treated at too close intervals, or if the serum is fortified with too large a dose of arsphenamin, anesthesia of the penis or rectum or bladder or numbness of the thighs will follow. The patient will state that he can retain urine for a longer time than usual and that he has movements without realizing that the rectum contains fecal matter. These symptoms are to be looked upon as a danger signal and treatment discontinued and not repeated until the condition has entirely cleared, when only the Swift-Ellis method should be resorted to. Weakness in the lower extremities and even complete paraplegia may result from too frequent repetition of the injection or the addition of too great a dose of the drug in reinforcing the serum.

It may appear superfluous to insist on accurate knowledge and experience before undertaking the procedure in question, but too much emphasis cannot be placed on such fundamentals. Every now and again reports come to me of partial or complete paraplegia and even death following intraspinal injections. It would seem as logical to blame cataract operations by the inexperienced for loss of vision as to incriminate the method in question wrongly employed for these disastrous results.

How long should antisyphilitic treatment be continued? In the absence of toxic drug symptoms and with proper rest periods the treatment may be continued until the blood and spinal fluid become negative. The dosage should be regulated by sex, age, body weight and occurrence or absence of reactive phenomena. It is better to err on the side of safety by giving too little rather than too much. The intervals for intravenous administration should be not shorter

than a week for the majority of patients, in some cases ten days to two weeks. Intraspinally never oftener than every two weeks for the first three or four injections, then at longer intervals. After six or eight treatments a rest period of two or three months.

After an experience of nearly seven years with both the Swift-Ellis and the reinforced serum it has been found that the former introduced by gravity is the better method and is followed by less reaction. The addition of ¼ mg. or more of arsphenamin where a number of injections have to be given will in some patients give rise to irritative symptoms, and the addition of smaller amounts has not shown any advantage over the serum obtained after an intravenous injection. It is also important to collect the serum not earlier than one-half hour after the injection. Experiments carried on with blood withdrawn immediately after injection or within fifteen minutes showed the arsenic content to be so high that bladder and rectal disturbances with numbness of the lower extremities resulted. The direct addition of neoarsphenamin or arsphenamin to the fluid is to be condemned (1) because the use of small amounts within a radius of safety is not productive of results, and (2) the employment of larger amounts is an exceedingly dangerous procedure. Small amounts of arsphenamin were used in my clinic over a period of months, and excepting some fluctuation in the cytology the method was barren of any benefit to the patient. The withdrawal of about 16 c.c. of spinal fluid and the medication of 30 to 40 c.c. in the gravity tube with the serum have given the best results.

In neurosyphilis developing within the first year of infection due to a local or disseminated meningitis the most brilliant results are obtained by the combined method. Cases of this nature are met with in patients who have had no treatment or are under treatment. The latter is exemplified in a young girl who had a primary lesion in May, 1919, a macular rash in June and placed herself under treatment in July. The latter part of October, while on a rest period after receiving nine arsphenamin and fourteen mercury injections, she developed a severe unilateral headache which troubled her day and night and would not yield to the administration of various headache remedies. She came under observation again on November 8, when a neurologic examination showed inequality of her pupils, with sluggish light reaction on the left side. The only change in the deep reflexes was in the left patellar, which was more active than the right. Her blood which was negative at the completion of her first course of treatment had again become positive, and a lumbar puncture made on the day of her return showed 16 cells; globulin, 4+; Wassermann, 4+ with 0.6 c.c., and a luetic curve with the gold sol. She was placed on combined therapy and after the second intraspinal injection the fluid became negative and has continued so. She received ten arsphenamin injections, three intraspinal injections and fifteen injections of mercury salicy-

late. Her blood and spinal fluid both became negative, but she was given an additional course of treatment and will remain under observation for the next two years. There have been no further subjective developments. The slight pupillary and patellar differences persist.

Another instance is that of a young soldier treated in the army for a chancre and secondary eruption with ten injections of arsphenamin and a course of mercury. When seen six months later he had a 2+ Wassermann reaction and no neurologic signs excepting a slight inequality of the deep reflexes of the lower extremities. After another course of arsphenamin and mercury he consented to a lumbar puncture. This revealed 15 cells; globulin, 2+; Wassermann, 4+, with 0.6 c.c. and a luetic curve. Under the combined treatment his fluid became negative after three intraspinal injections.

Case 3 is Dr. X., who infected both index fingers while performing a tonsillectomy. Late in April, 1919, the diagnosis of primary lesions was made and treatment immediately instituted. He took seven injections of arsphenamin and twenty-four injections of bichloride of mercury, gr. $\frac{1}{10}$, then potassium iodide up to grs. 60 t. i. d.; after which another course of six injections of arsphenamin, 0.6 gm., twenty-four injections of bichloride and potassium iodide for six weeks. The latter part of September, 1919, he developed intense temporal headache with projectile vomiting. Again he took four injections of arsphenamin, 0.6 gm., and 10 rubs, following which up to January an occasional dose of arsphenamin and mercury and iodide by mouth. At this time he developed an iridocyclitis and received four injections of neoarsphenamin, 0.6 gm.; which had a beneficial effect on the pain and congestion. He came under my observation March 25, at which time it was found he had no vision on the temporal side of the left eye. The left pupil was larger than the right and sluggish to light, otherwise neurologic and physical examinations were negative. His serologic findings and treatment were as follows:

CEREBROSPINAL FLUID.

Date.	Cells.	Globulin.	Wassermann.	Gold sol.	Serum.
Mar. 27, 1920	67	++++	++++ to 0.6	2332100000	April 10, 1920 ±
April 14, 1920	102	++++	++++ to 0.6		
May 5, 1920	15	+	++++ to 0.6	1121100000	
May 26, 1920	7	+	++++ to 1.5		
June 23, 1920	4	±	+++ with 2.0	1111000000	June 23, 1920 ±
July 28, 1920	4	±	− with 2.0	0000000000	July 28, 1920 −

Treatment from April 8 to July 28, 1920: Five intravenous injections of arsphenamin and five intraspinal injections, Swift-Ellis.

Results. The eye remains the same, the ophthalmologic report being that the floating exudate of the original iridocyclitis is the same in amount and opacity. The vision corrected with a 50-diopter lens has given relief to the headache due to eye-strain.

Many cases of this character might be cited showing the rapidity with which disease of the central nervous system in its inception responds to the combined treatment, necessitating frequently only three to ten intraspinal injections to bring about complete recession of clinical and serologic symptoms. When we compare these results with those after degenerative changes have set in and the Wassermann is practically fixed the value of early treatment is obvious. Speculating as to the future outcome of these patients if a negative Wassermann in the blood alone were depended upon and a *laissez-faire* policy adopted as to the significance of a positive spinal fluid, one can easily visualize them as victims of tabes, optic atrophy, paresis or other types of neurosyphilis.

The following cases of early neurosyphilis treated by spinal drainage are inserted because the first is the only one we have had to date show any decided change in the spinal serology and the other because it shows the usual result with this method.

J. B., aged twenty-eight years. Chancre in November, 1919, followed by adenopathy; no rash. Wassermann, ++++. After receiving eight injections of arsphenamin and eight of mercury he left the city. In February, 1920, he developed an iritis; a week later, tinnitus and slight deafness. The following week a right-sided facial palsy and two days later paralysis of the left side of face, but not quite so marked. He returned to the clinic on March 16, 1920, at which time a neurologic examination revealed very active deep reflexes on both sides, more marked on the left. There was no clonus or Babinski; slight Romberg was present. His pupils were equal, round and reacted normally to light and accommodation. The right side of the face was paralyzed and the left showed flattening, with weakness of the muscles innervated by the seventh nerve.

CEREBROSPINAL FLUID.

Date.	Cells.	Globulin.	Wassermann.	Gold sol.	Serum.
Mar. 24, 1920	210	++++	++++ to 0.4	5533211000	Mar. 24, 1920 ++++
April 29, 1920	200	++++	++++ to 0.4		
May 18, 1920	50	trace	++++ to 0.8	2233210000	
May 29, 1920	5	trace	++++ to 1.5		
June 16, 1920	4	trace	++++ to 1.5		
July 3, 1920	4	trace	++++ to 1.5	....	July 3, 1920 −
July 16, 1920	4	trace	++++ to 1.5	1232100000	

Eight weeks after the last drainage the spinal fluid again became strongly positive, showing cells, 200; globulin, 3+; Wassermann, 4+ with 0.1 c.c., and a paretic curve with the gold sol.

Treatment from March 16, 1920, to July 16, 1920: Twelve intravenous injections of arsphenamin; eight spinal drainages, each about an hour after an intravenous injection; ten injections of mercury.

All his symptoms entirely disappeared excepting a slight flattening and weakness of the right side of the face. The amount of globulin in the spinal fluid, although indicated as 4+, was greatly in excess of that usually found, the fluid coagulating almost solid on the addition of the reagents. This rapidly cleared up. To this excessive amount might also be attributed the paretic curve and its rapid conversion to luetic with the diminution of the globulin. The Wassermann in the spinal fluid has not yielded as rapidly as in cases when the serum is introduced.

R. O., aged thirty-five years. Chancre on October 20, 1919; no rash. Wassermann, ++++. Treatment: eight injections of arsphenamin and eight injections of mercury, when patient discontinued because he could no longer get away from work. About March 25, 1920, he developed severe occipital headaches, which were worse at night. He returned for further treatment on April 7. His pupils were equal, regular in outline and responded promptly to light and accommodation. His deep reflexes were all active and equal on the two sides.

CEREBROSPINAL FLUID.

Date.	Cells.	Globulin.	Wassermann.	Gold sol.	Serum.
April 9, 1920	220	++++	++++ to 0.1	5555432100	Nov. 3, 1919 ++++
April 12, 1920	200	++++	++++ to 0.1		
April 26, 1920	100	++++	++++ to 0.1		
May 17, 1920	80	++++	++++ to 0.1		
June 16, 1920	60	++++	++++ to 0.1		
June 28, 1920	50	++++	++++ to 0.1	5555432100	June 25, 1920 +

Treatment from April 12 to June 28, 1920: Eleven intravenous injections of arsphenamin; five spinal drainages, each about one-half to one hour after an intravenous injection; six injections of mercury.

Arguments as to the superiority of the intravenous as compared with the intraspinous method are more or less valueless and futile. A wide grasp of syphilis as a general infection, a knowledge of the biologic reactions of the blood and spinal fluid, with sufficient experience to intelligently interpret and correlate them with the signs and clinical symptoms, are essential prerequisites before one is in a position to express a critical opinion.

The results we have obtained during many years of careful work have convinced us beyond the shadow of a doubt that much more

can be accomplished by the method in question in properly selected cases than by intravenous treatment alone.

The group of neurosyphilitics who have been treated intensively by the intravenous method alone with limited or no improvement give some of the best results which have been achieved by intraspinal treatment.

To substantiate this statement the two following cases of optic atrophy are appended:

Dr. Z., a dentist, gave no history of syphilis but had complained of recurring attacks of severe pain in his left eye and back of the neck for several years, the cause of which was not diagnosticated until about a year ago, when he consulted a physician for his failing vision. A Wassermann made at that time was found to be positive as was also his spinal fluid. He placed himself in the care of a competent neurologist and received sixteen injections of arsphenamin intravenously, together with mercury. His vision during the treatment continued to fail until it was lost altogether in the left eye and was rapidly disappearing in the right. He had been obliged to give up his work and could only read very large print in a strong light. A lumbar puncture made on January 24, 1920, revealed 182 cells; globulin, 4+; and Wassermann, 4+ to 0.1 c.c. with a paretic type of curve. On combined therapy his right eye so improved that he was able to resume his profession and also read the paper again. He had seen several ophthalmologists who gave him an absolutely bad prognosis, with complete blindness as the only outcome. On January 14 he consulted Dr. Weeks. A letter from the latter's associate, Dr. Steese, under date of March 8, reads: "Dr. Z., on January 14, showed complete atrophy of the left optic nerve and partial atrophy of the right. Vision of latter was 20/70, left nil. There was no improvement possible." On March 15 Dr. Steese reported: "Dr. Z.'s vision today without glasses: Right eye, 20/50, with −0.75 20/40. This is a great improvement over his visit of January 14, when vision was scarcely 20/70. The left eye can now perceive movements in the outer quadrant." A message from the patient in October stated that his vision continued as in January.

The second patient, aged twenty-eight years, had had a chancre in 1911 followed by secondaries, for which he received a course of injections of gray oil each year. In April, 1918, he noticed gray spots in front of his right eye. Two months later vision began to fail and three months after he was totally blind in the eye. He was treated with arsphenamin intravenously for several months. On February 1, 1919, he complained of cloudiness of vision on the left side. Examination on February 14, 1919, showed the right pupil larger than the left; light and accommodation reflexes absent on the right side; sluggish on the left. Dr. Knapp reported vision 20/30, with temporal contraction of field. His reflexes were more

active on the left side. No Babinski or clonus. Superficial reflexes active. His spinal fluid examined February 18, 1919, showed cells 32; globulin, +++; Wassermann, ++++ to 0.4 c.c.; gold sol, 1233210000. His blood was +++. He was given twelve intravenous injections and eight intraspinal injections along with thirty-five injections of mercury intramuscularly. Owing to the development of jaundice, treatment was interrupted for several months.

Results. On October 15, 1919, Dr. Knapp reported: "While the sight of his only eye remains good there seems to be a contraction of his field particularly for colors on the temporal side." March 2, 1920, Dr. Knapp wrote: "Vision, 20/30; pupil somewhat dilated; reacts slightly; optic nerve pale; vision the same as one year ago." Because of the rapid development of the atrophy in his right eye it is fair to assume that treatment is responsible for arrest of the progress in the left eye. His spinal fluid and blood are negative.

It is poor judgment, to express it mildly, to treat rapidly progressing optic atrophy intravenously without definite knowledge of the spinal fluid. Positive findings, including a high cell count, point to a basilar meningitis, a condition readily influenced by intraspinal medication. Records of twenty cases treated intraspinally show arrest of the atrophy. Why permit such patients to progress to complete blindness when experience shows in certain cases that progress of the atrophy can be absolutely arrested? A patient with a progressive optic atrophy and a positive spinal fluid is not receiving proper or adequate treatment by intravenous therapy alone. Claims made that the remedy cannot reach the diseased optic nerves when introduced in the lumbar subarachnoid space are absolutely untrue and disproved by the clinical results and fluid tests. The first case herein quoted, which is only one of a number of similar ones, had received sixteen injections of arsphenamin intravenously, in spite of which he lost the sight of his left eye and was rapidly losing that of the right; his spinal fluid showed a cell count of 182, indicating that his meningitis was not responding to the treatment given. After two intraspinal injections a decided improvement occurred in the right eye and the cell count was reduced to 22.

Conclusions. A definite and constructive plan for the prophylaxis of the degenerative stage of syphilis of the central nervous system and its treatment in the initial stages can only be devised by a study of the infection in its inception. Our clinical and serological work during the past ten years have enabled us to formulate the following propositions:

1. Syphilis of the nervous system probably begins in the first year of the infection. The number of cases corresponds roughly with the total number of cases of so-called late neurosyphilis. The foregoing statements are based on the following observations and established facts: (*a*) The number of early cases showing positive

findings in the spinal fluid; (*b*) familial types of neurosyphilis; (*c*) biologic evidence of a neurotropic strain of the treponema; (*d*) persistence of the infection *in loco*, as in aortitis, interstitial keratitis, etc.; (*e*) observation of patients who developed signs of early syphilis of the nervous system and who after many years died of paresis or other late degenerations; (*f*) no serologic evidence as yet exists showing normal spinal fluid in the early stage and its infection at a later period.

2. Early neurosyphilis may manifest itself by obtrusive symptoms by slight objective signs or be asymptomatic. Treatment by the usual channels may control the obtrusive symptoms. It seldom cures the underlying infection. Symptoms at times develop during or shortly after intensive courses of arsphenamin and mercury. If not cured these early infections may persist and cause late neurosyphilis.

3. Acceptance of the foregoing propositions leads to the logical deduction that no case of syphilis should be discharged without the knowledge gained by examination of the spinal fluid. In case no evidence of infection is found a prognosis of probable future immunity may be made. If infection exists it should be treated by methods shown by experience to be effective.

4. We are convinced by an experience of seven years in the use of intraspinal therapy that practically all cases of early neurosyphilis can be cured more rapidly, and in the majority of cases only cured, by the combined intravenous and intraspinal method.

THE EFFECT ON BLOOD-PRESSURE AND THE NON-PROTEIN NITROGEN IN THE BLOOD OF EXCESSIVE FLUID INTAKE.[1]

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and

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The nitrogen excretion in nephritis is generally thought to bear a certain relationship to the quantity of urine excreted. Bamberger taught that flushing out the kidney increased the urea elimination. Mohr[2] in von Noorden's clinic later, concluded that reduction of fluid to the point where the daily output of urine fell below 1200 c.c. often led to urea retention. On the other hand the maximum

[1] Read before the Association of American Physicians, Atlantic City, May 4, 1920.

[2] Beiträge zur Diatetick der Nierenkrankheiten, Ztschr. f. klin. Med., 1903, l, 377.

nitrogen elimination was obtained with a daily excretion of 1500 c.c. of urine. Von Noorden strongly urged that excessive quantities of fluid be avoided on account of the danger of raising the blood-pressure. He advised that the fluids be restricted sufficiently to maintain a daily output of 1500 c.c. of urine and as a safeguard once a week a flushing-out day where the fluid intake is increased to the point where the primary output reaches 2 to 3 liters.

This teaching of von Noorden has been quite widely accepted although many have questioned whether the apprehension regarding the danger of raising the blood-pressure by increased fluids was well grounded. This is due to the physiological experiment that in the laboratory animals an intravenous injection of salt solution equivalent to 50 per cent. of the blood volume produced only a slight increase in the blood-pressure. With properly functioning kidneys this probably holds true in man.

Recently, Foster and Davis[3] have studied 22 cases of nephritis determining the effect of water drinking on urea excretion. As a result of these observations they concluded, subject to individual variation, that when the daily output of urine was reduced below 1000 c.c. nitrogen retention resulted. The amount of urea excreted increased with the fluid taken and when the urinary excretion reached 2000 c.c. daily the nitrogen output exceeded the intake.

Minkowski[4] in reviewing the effect of water drinking in gout found considerable difference of opinion regarding its value in the elimination of uric acid. He considered that the maximum benefit is derived when 1½ to 2 liters are taken in the twenty-four hours.

It was thought that it might be of interest to determine whether by increasing the fluid intake to a very high point by use of the Rehfuss tube the nitrogen elimination could be increased as shown by the reduction in the non-protein nitrogen in the blood. At the same time the effect on blood-pressure of high fluid intake could be observed. The observations were carried out on three patients. Two were cases of hypertension. One had only a very slight increase; the other a very decided increase in the non-protein blood nitrogen. Both had nocturnal polyuria and at no time had shown evidence of edema, although both came to the hospital on account of dyspnea on exertion. Apparently they both eliminated water well through the kidney. The urine contained an inconstant trace of albumin, and an occasional hyalin and granular cast. The third case was a typical, chronic gout of ten years' duration. The fingers showed to a very high degree the characteristic deformities. There were urate deposits in the ear cartilages and a large collection of urates in the olecranon bursæ. He no longer had any typical acute exacerbation, but rather prolonged periods of increased discomfort followed by weeks of comparative ease. The blood-pressure was

[3] The Effect of Water Intake on Nitrogen Reaction in Nephritis, Am. Jour. Med. Sc., 1916, cli, 49.

[4] Gicht, 1901.

only moderately elevated, 165 systolic. The urine did not contain any albumin or casts.

During the period of observation all these patients were on the hospital nephritic diet which includes all the carbohydrate foods. In the portions ordinarily served this diet contains between 50 and 60 grams of protein.

The non-protein nitrogen of the blood was determined twice at intervals of four or five days preceding the water drinking test. The mean of these two readings was taken as the average. The water was introduced through the Rehfuss tube, the patient being given 2½ liters every three hours from 9 A.M. to 6 P.M. or a total of 10 liters daily. This was continued for six days and twenty-four hours after completing the test the non-protein blood nitrogen was again determined. The time consumed in taking any one portion of fluid, *i. e.*, 2½ liters, varied from fifteen to twenty-five minutes.

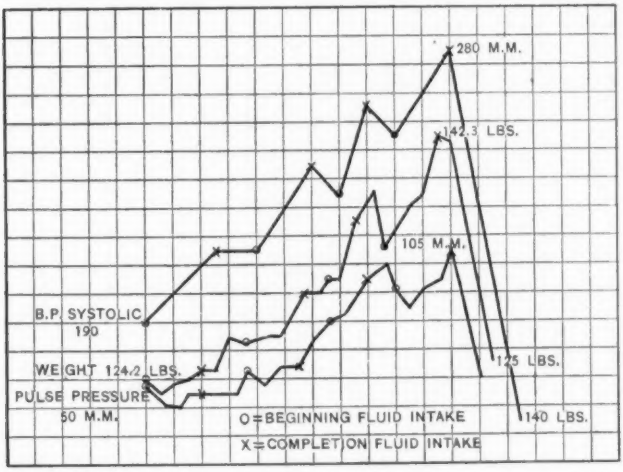
The retention of the water was determined chiefly by repeatedly weighing the patient. The urinary output for the various periods was also recorded.

PROTOCOL I.

	Time.	Systolic.	Diastolic.	Pulse pressure.	Weight, pounds.	Urinary output.
Dec. 20, 1919						
First 2½ liters:						
Before taking.	9.00 A.M.	160	108	52	124.2	
¼ taken . .	9.15 A.M.	150	100	50	....	9 to 12 A.M., 850
½ taken . .	9.27 A.M.	155	110	45		c.c. clear urine
¾ taken . .	9.35 A.M.	158	110	48		voided.
At completion	9.42 A.M.	162	115	47	129.2	
½ hour later .	10.15 A.M.	162	115	47		
1 hour later .	10.40 A.M.	180	120	60		
Second 2½ liters:						
Before taking.	12.00 P.M.	175	120	55	128.6	From noon till 3
¼ taken . .	12.10 P.M.	180	123	57		P.M.
½ taken . .	12.17 P.M.	180	123	57	....	1400 c.c. clear,
¾ taken . .	12.22 P.M.	188	130	58		pale urine
At completion	12.40 P.M.	205	145	60	134.0	voided.
1 hour later .	1.30 P.M.	205	132	73		
Third 2½ liters:						
Before taking.	3.10 P.M.	210	115	95	132.2	From 3 to 6 P.M.,
¼ taken . .	3.20 P.M.	210	125	85		1575 c.c. of
½ taken . .	3.43 P.M.	230	140	90		urine voided.
At completion	3.50 P.M.	242	142	100	137.5	
1 hour later .	4.40 P.M.	255	150	105		
Fourth 2½ liters:						
Before taking.	6.00 P.M.	225	130	95	136.3	
¼ taken . .	6.10 P.M.	230	140	90	....	From 6 to 9 P.M.
½ taken . .	6.17 P.M.	240	145	95		of the next day,
¾ taken . .	6.25 P.M.	255	155	100		8600 c.c. of
At completion	6.35 P.M.	287	180	107	142.3	urine voided.
1½ hours later	8.00 P.M.	280	180	100		
Dec. 21, 1919.	9.00 A.M.	140	90	..	125.8	

I. K., aged thirty-five years, had been in the county hospital repeatedly during the past three years. His chief complaint had been dyspnea on exertion, which rapidly subsided with a moderate degree of physical quiet. His systolic blood-pressure was usually above 200. The maximum reported was 250. There was no evidence of edema. The urine contained an inconstant trace of albumin and an occasional granular or hyaline cast. His phthalein output in three hours was 80 per cent. His urea nitrogen was 24.28 mg. per 100 c.c. of blood. The total non-protein nitrogen was 40.83 mg. Protocol I gives the record for one twenty-four-hour period:

Patient had no bowel movement during the time these data were being taken. At the end of the third five liters he complained of



Showing changes in blood-pressure and weight with each successive fluid intake and the level twelve hours later.

headaches and dizziness, which continued throughout the night. Claims he did not sleep during the entire night because of headaches, dizziness and general depression, with frequent urination. Meals were taken at 11 A.M., 5 P.M., and 8 A.M.

Summarizing the results in this table the systolic and diastolic pressure rose steadily, with the exception of temporary remissions between fluid intake periods from the beginning to the end of the test. The systolic pressure increased from 160 to 287, the diastolic from 108 to 180 and the pulse-pressure from 55 to 107. His increase in weight from the beginning to the end of the experiment was 18.1 per pound. The following morning the weight had fallen to within 1.6 pounds of that preceding the experiment. He first began com-

plaining of headache and dizziness about one hour after completing the second 2½ liters, which corresponds closely to the increase in pulse-pressure. During the other five days of the test he invariably complained of headache at this same period. At no time was there any visible subcutaneous edema. That the volume of the blood was probably definitely increased is shown by the pulse-pressure. The urea nitrogen twenty-four hours after this six-day period of water drinking was 25.5 mg., the total non-protein nitrogen 37.2 mg. as compared with 24.28 and 40.83 mg. before the test. The uric acid was 3.08 before and 1.51 after. The creatinin was 1.56 mg. before and 1.48 mg. after the test. The urea nitrogen actually increased slightly while there was a small reduction in the total nitrogen. These changes, however, may be considered negligible, as they represent only the normal variations. The reduction in the uric acid would appear to have been the result of the treatment, as a week after it was discontinued the uric acid had increased to 2.05. During the week following the patient was given the same amount of water during one night in order to see if the retention of fluids would be the same as during the day.

PROTOCOL II.

Water was given during the night of December 26 and 27, 2½ liters at three-hour intervals as usual, with the following results:

	Time.	Systolic.	Diastolic.	Pulse pressure.	Weight, pounds.	Urinary output.
First 2½ liters:						
Beginning	6.00 P.M.	170	100	70	131.7	6 to 9 P.M., 1180
¼ taken	6.05 P.M.	175	105	70		c.c. pale urine
½ taken	6.13 P.M.	185	115	70		voided.
At completion	6.25 P.M.	210	120	90	137.2	
2 hours later	8.00 P.M.	185	115	70		
Second 2½ liters:						
Beginning	9.05 P.M.	190	110	80	134.2	From 9 until
¼ taken	9.11 P.M.	195	115	80		midnight, 1800
½ taken	9.15 P.M.	210	120	90		c.c. of urine
At completion	9.27 P.M.	220	120	100	139.0	voided.
Third 2½ liters:						
Beginning	12.07 A.M.	180	100	80	134.0	From midnight
¼ taken	12.13 A.M.	205	115	90		until 3 A.M.,
½ taken	12.30 A.M.	220	120	100		1950 c.c. urine
All taken	12.30 A.M.	230	130	100	138.9	was voided.
Fourth 2½ liters:						
Beginning	3.05 A.M.	225	130	95	135.5	3 to 6 A.M., 2760
¼ taken	3.15 A.M.	225	130	95		c.c. voided.
½ taken	3.19 A.M.	230	130	100	....	6 to 9 A.M., 1900
At completion	3.25 A.M.	260	155	105	140.6	c.c. voided.
At	9.00 A.M.	180	105			
Later	12.00 A.M.	160	100	..	....	Noon till 3 P.M., 1330 c.c. voided.
Later	3.00 P.M.	140	90	..	133.0	1140 c.c. voided.
Dec. 28, 1919.	11.00 A.M.	155	90			

The maximum systolic pressure was somewhat less during the night than during the day experiment (260 as compared with 280). That the water was eliminated much more readily at night is shown by the gain in weight which was 8.9 pounds.

The second patient tested was clinically similar to No. 1, with the exception that the non-protein nitrogen was high. The systolic blood-pressure ranged around 200. The urine contained a trace of albumin and an occasional hyaline and granular cast. The urea nitrogen was 56 mg.; the total nitrogen, 72.9 mg.; uric acid, 6.59 mg.; creatinin, 3.3. On account of the marked distress following 5 liters of fluid the patient was given 7500 c.c. daily the first two days and 5 liters daily the remaining four days.

PROTOCOL III.

	Time.	Systolic.	Diastolic.	Pulse pressure	Weight.
Dec. 2, 1920.					
First 2500 c.c. of tap water:					
Beginning	9.20 A.M.	200	104	96	137.75
¼ taken	9.25 A.M.	198	115	83	
½ taken	9.36 A.M.	206	96	110	
All taken	9.40 A.M.	204	122	82	142.25
2 hours later	11.30 A.M.	206	110	96	
Patient felt a little dizzy immediately, but it wore off soon. Before the next dose he passed 600 c.c. of urine; sp. gr., 1008 and had a bowel movement.					
Second 2500 c.c. of tap water:					
Beginning	12.52 P.M.	208	120	88	142.00
¼ taken	1.00 P.M.	208	110	98	
½ taken	1.10 P.M.	212	125	87	
All taken	1.16 P.M.	206	140	66	146.00
2 hours later	3.10 P.M.	198	120	78	
Patient was a little restless and dizzy immediately, but no worse than after the first dose. Before the third dose he passed 1200 c.c. of urine of 1006 sp. gr.					
Third 2500 c.c. of tap water:					
Beginning	5.00 P.M.	210	125	85	142.50
¼ taken	5.03 P.M.	210	132	78	
½ taken	5.10 P.M.	220	135	85	
All taken	5.15 P.M.	230	140	80	146.00
2 hours later	7.00 P.M.	242	120	122	

Immediately after this he felt restless and dizzy and complained of a feeling of fulness in the abdomen, but did not seem worse than after the other two doses. However about one hour later he had a severe chill with nausea, vomiting, dyspnea, headache and cramps in his legs. This lasted all night, but by morning he was all right. Urine, 2100 c.c.; sp. gr., 1004.

In this patient the systolic blood-pressure rose from 200 to 242; the diastolic from 104 to 140. The pulse-pressure showed extreme variation, reaching its maximum of 122 at the end of the test. The increase of weight was 9¼ pounds. This patient complained of dizziness following the administration of each portion, and one hour after the third portion had a chill with vomiting and cramps in the leg. For this reason no attempt was made to increase the fluid beyond 7500 c.c. The day following the same symptoms following the third portion and in the few following days only 5000 c.c. was given daily. The urea nitrogen before the test was 56 mg.; the non-protein nitrogen, 72.9 mg.; uric acid, 6.6. mg.; creatinin, 3.3 mg. Twenty-four hours after completion of the six days' test the urea nitrogen was 54.1 mg.; the non-protein nitrogen, 69.6 mg.; uric acid, 5.9 mg.; creatinin, 2.45 mg. The slight reduction in the urea nitrogen and total nitrogen is probably negligible as variations of this degree occur normally.

The third patient was a high-grade chronic gout of ten years' duration. His phthalein output was 12 per cent. in three hours. Systolic blood-pressure ranged from 150 to 170.

This patient took 10 liters of water daily for six days without inconvenience. He eliminated the fluid almost as rapidly as it was taken. The maximum increase in blood-pressure was 15 mm. and he did not show any appreciable gain in weight.

The urea nitrogen before the test was 66 mg.; after the test 69.4 mg. Total non-protein nitrogen before the test, 92 mg.; after the test, 97 mg. Uric acid before, 8.25 mg.; after, 4.85 mg.

This shows a very definite reduction in the uric acid, but an increase in the urea nitrogen and total nitrogen. It is highly probable that this reduction in the uric acid was the result of the treatment as repeated determination of uric acid previous to and following the test had never fallen below 6.25 mg. per 100 c.c. of blood. One week after the test the uric acid had increased to 9.17 mg. This is in accord with what occurred in Case I where there was a very definite decrease in the uric acid, but without change in the urea nitrogen. The patient with gout, however, in a later test where he was given 10 liters of water daily for eight days, showed a slight increase in the uric acid in the blood from 6.17 to 7.25 mg. per 100 c.c. Atophan, 3 gms. daily for one week, did not reduce the amount of uric acid in the blood.

We wish to acknowledge the valuable assistance rendered by the interns on the service at Cook County Hospital.

Summary. In patients with hypertension and presumably chronic interstitial nephritis, large amounts of fluids may cause a very decided increase in blood-pressure. Whether this rise occurs depends upon the promptness with which the kidneys function in excreting water.

In the three cases studied the taking of large amounts of fluid

daily for a period of six days was without effect on the urea nitrogen in the blood. As it was not feasible to determine the nitrogen eliminated in the urine during this period these results do not exclude the possibility of increased nitrogen output.

In two of these three cases the uric acid in the blood was definitely lessened. This was probably due to the treatment as following its discontinuance there was an increase to the previous level.

PROBLEMS CONCERNING URINARY CALCULI.[1]

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Urinary calculi consist of agglomerations of non-acicular crystals about a nucleus of organic matter. Concentration of the urine in the presence of pus or blood due to trauma or disease must be the occasion of stone formation. But with the exception of the secondary calculi, obviously due to inflammation, this bare fact has not elucidated the cause of stone. One would expect that trauma to the kidney should be a frequent cause of bleeding calculated to result in stone; yet such does not seem to be the case. Prize fighters are not notoriously subject to stone, and in reviewing a series of some 200 cases of primary renal stone, I find but 5 in which the symptoms of stone began within a few years after a trauma.

It is more profitable then to accept the fact that stones do begin and to study the clinical features they present that seem to bear upon their origin.

Most primary stones contain both urates and oxalates. But in contrasting bladder and renal calculi we are immediately struck with the predominance of urates in the stones found in the bladder and the predominance of oxalates in renal and ureteral stones. By the same token the former frequently fail to show by roentgen ray while the latter are but rarely overlooked. Thus in a consecutive series of cases in which stone was present the radiographic results were as follows:

	Positive.	Erroneously negative.
Renal pelvis	32	6
Ureter	20	14
Bladder	16	12

Most of the failures to show ureter stone are attributable to the small size of the stone and many of the successful pictures of bladder stones to the presence of phosphates.

Bladder stones are disproportionately frequent in childhood, corresponding with the predominance of urate deposition in the

[1] Read before the Association of Genito-Urinary Surgeons, May, 1920.

urine of the young, while adults show a more marked tendency to the urinary precipitation of oxalates.

A majority of the urate stones retained in the bladder have no antecedent history of renal colic. Does this mean that urate stones more commonly form in the bladder while oxalate stones more often form in the kidney pelvis? Probably not. Let us not forget that the urologist is not really concerned with stone as such but only with such stones as fail to pass from the urinary channels or in passing excite symptoms. Many very small stones doubtless pass silently. We are interested only in those that grow so large they cannot do this. And this means retention.

There are four ways in which a stone may be retained in the urinary channels, viz.:

1. The stone may adhere to its point of formation until too large to pass.
2. It may be irregular in shape and thus peculiarly liable to catch in ureter or urethra.
3. It may lie in some part of the pelvis of the kidney or bladder where it does not present at the ureteral or urethral orifice.
4. There may be ureteral or urethral obstruction (*e. g.*, stricture).

1. *Adhesion to the point of origin* may be actually observed in the case of secondary bladder stones. A similar process may delay the discharge of certain primary renal stones, for sometimes we recover small oxalate stones (after they have passed noisily down the ureter) which show a cup shape, as though they had remained for some time adherent to the tip of a renal papilla; indeed, such adhesion has been observed postmortem.

2. Comparison of the size and shape of stones passed after renal colic with the difficulty of their passage will confirm the rather obvious assumption that *it is the shape rather than the size* that determines the likelihood of the stone being caught and temporarily or permanently impacted in the ureter.

Is not this the reason why we, who are interested only in impacted or retained stones, find oxalates predominating in the upper and urates in the lower urinary channels? It would seem so. At least I know of no change that the urine undergoes in passing from the kidney to the bladder that would make it more likely to form urate stones in the latter while the smooth urate stone may certainly slip silently down the ureter that would react in violent spasm to the passage of a jagged oxalate stone even smaller in size. But once the stone reaches the bladder the probabilities are reversed. Here the very roughness of the oxalate stone facilitates its discharge by exciting contractions that no smooth stone would evoke.

3. *Retention* explains several facts in relation to stone. The silent stone filling the pelvis of the kidney has had its beginning as a small stone lying in one of the lower calices until it has grown over the orifice of the ureter. Such silent stones are also found in the

bladder and even in the ureter and the urethra. In the bladder they imply at least a little retention of urine (perhaps the same is true of the kidney) and in the narrow passages the silent stone is usually found behind a stricture.

By means of the roentgen ray I have actually watched the growth of a secondary renal stone (whose rate of growth is much more rapid than that of a primary stone) in seven years from a maximum diameter of 0.5 cm. to 5 cm.; and in my precystoscopic days I watched a patient, who suffered only from a slight hematuria when he rode horseback, for three years before the roentgen ray revealed two stones in his bladder, each of them 3 cm. in its smallest diameter.

In the ureter I have known a stone to cause a severe colic and then remain entirely silent for five years. Another ureteral stone (following trauma to the loin) produced attacks of pain of varying severity for fifteen years (approximately) and thereafter for twelve years only hematuria when the patient rode horseback. Another grew to be 1 cm. long and never gave a symptom.

In the urethra I have known a stone to grow (behind a tight stricture) to a size almost that of the last joint of the thumb without exciting a symptom of which the patient was willing to complain—indeed, he entered the hospital for the treatment of rheumatism and his stone was disclosed by the routine examination.

Perhaps the best testimony to the influence of retention upon stone is the fact that I have never seen a primary stone retained in the bladder of a woman and but one in the female urethra.

Renal Colic.—The following table collected from my case records shows the age at which the first colic or pain proved due to ureteral or renal stone was felt:

Age at first colic.	Cases.
Birth to 10 years	6
11 to 15 years	1
16 to 20 "	13
21 to 25 "	21
26 to 30 "	30
31 to 35 "	28
36 to 40 "	32
41 to 45 "	20
46 to 50 "	21
51 to 56 "	17
57 to 60 "	7
61 to 65 "	3
66 to 70 "	0
71 to 75 "	2
Total	201

This table may be summarized by the statement that only one in ten of the patients began to have renal colic before the age of twenty, yet one-half had begun before thirty-five; the peak is between the ages of twenty-six and forty; the odds against beginning to have renal colic after the age of fifty are about twenty to five.

These statistics were gathered from 244 patients proved to have urinary stone, presumably primary in the kidneys. In 225 there was evidence (pain) that the stone had originated in the pelvis of the kidney. There were only 11 cases of "silent" stone (two bilateral), 3 with only mild pain and bleeding and 5 with toxic symptoms exclusively.

Having a distinct impression that the mobility of the right kidney should make renal colic definitely more frequently upon the right side, I was disappointed to find, after tabulating 178 cases, that 90 occurred upon the left and 88 upon the right side. The statistics of Braasch and of Cabot confirm this observation.

But we are more immediately interested in the practical questions relating to renal colic. When a stone jams in the ureter, what is the best method of relieving the colic and of expediting the passage of the stone? How shall we know that the stone will not pass? And if the jam is thus permanent, in what portion of the ureter is it most likely to occur?

There seems to be a general impression abroad that colic expedites the passage of stone through the ureter. At any rate we commonly speak of the passage of stone following a colic. Yet, considered as a mechanical proposition, a renal colic is rather the outcry of the outraged, overdistended urinary channels than a coördinated effort to expel a foreign body. It may conceivably benefit the sufferer little more than a cramp in the leg does a swimmer. It would be more accurate to look upon the cessation of colics as the evidence of the passage of stone. Commonly the stone seems to leave the ureter with a colic, but close observation will bring to one's notice many instances in which the stone leaves the ureter without a colic. I have observed two very striking examples of this, in each of which the stone passed without colic, and indeed under conditions that precluded the possibility of colic. And these stones were above the average in size.

Case I.—The patient was a stout, middle-aged Russian who had paid as little attention as possible to the renal colic from which he had suffered for several years. Finally his infected renal pelvis ruptured, but even then he did not call a physician until he was so nearly dead from sepsis that the first surgeon summoned to his bedside deserted him, with the cheering information to the family that the "patient would be dead by morning." But the infection was an acute one and the patient a sturdy type. I drained his loin, he recovered and is alive and at work today, though suffering from renal insufficiency, it being now fifteen years since the operation. But the startling feature of his case is that on the fifth day after operation he passed from his bladder a stone, 1 x 2 cm. in diameter. The kidney was draining freely into the loin at the time and he had not the least ureteral pain to announce the passage of the stone, though it passed through the urethra with some difficulty.

CASE II.—A similar case. I was called out of town to operate upon a man who after a single renal colic had been in calculous anuria for several days. Bilateral simultaneous nephrotomy drew several stones from the left renal pelvis. The right yielded only urine under great pressure. It was deemed safer not to attempt any further exploration; yet on the sixth day of his uneventful convalescence he passed a stone about 0.5 cm. in its smallest diameter and without any ureteral colic. Subsequent radiograms were negative and he had no further symptoms of stone in the two years that elapsed before I lost sight of him.

Since these two cases called my attention to the possibility of the passage of ureteral calculi without pain I have confirmed the observation several times.

CASE III.—Thus last summer I took charge of a woman who having lost her right kidney the year before (nephrectomy for stone) had been in bed for several weeks suffering from urinary septicemia, with recurring chills and fever and loin pain of considerable severity. I promptly transferred her to a hospital, where the roentgen ray revealed a small stone at the lower end of the left ureter. I thereupon by abdominorectal palpation felt the stone and endeavored to dislodge it. Neither she nor I believed I had accomplished anything, but when I visited her the next day her temperature was down, the loin pain had ceased and she assured me that she felt the stone in the bladder. The following day she passed it. She remains well today (a year later).

Such observations as these suggest that a stone—even a large stone—may pass from the ureter without colic. They also suggest, as previously stated, that the colic is comparable from various points of view to the cramp in the leg of a swimmer.

What then should we do in the presence of renal colic? Kill it. I have tried to do this with various of the substitutes for morphin. None of them has given me any satisfactory results. General anesthesia is the only competitor. I have no reluctance about giving the drug freely. One of my interns took 25 minims of Magendie's solution one night before he got rid of his renal colic; and he seemed little the worse for wear the following day. In short, I advocate the administration of morphin, not out of sympathy for the patient's suffering but because it relieves the spasm that is surely doing little good, may do harm and without which the patient can perfectly get rid of his enemy.

Among the mechanical aids to the passage of ureteral stone I cannot name one for which I have any very great preference. If the stone is at the lower end of the ureter I always attempt to help it along by recto-abdominal manipulation, and have thus twice delivered stones into the bladder. I have had no success with the various fluids recommended for injection into the ureter, and the

only ureteral operation that has shown any promise in my hands is one I hesitate to recommend, as it seems so fantastic. If the stone is arrested near the lower end of the ureter, even though it be several centimeters from the bladder orifice of the canal, I believe its ultimate expulsion is expedited by cutting open the urethral orifice with the cystoscopic scissors or forceps. The ureter catheter itself, of course, occasionally dislodges a stone. I believe that I have eight times expedited the passage of ureteral stones by mechanical measures.

How shall we decide that a stone is permanently lodged in the ureter? This, the most important of all the problems in relation to the surgery of ureteral stone, cannot be answered categorically.

Case IV.—I was once consulted by a patient who was most anxious not to be operated upon for six months, although the roentgen ray had shown a small stone in the upper part of his right ureter.

His only colic had occurred the week before. It seemed possible that the stone would pass, and inasmuch as the ureter catheter not only verified the location of the stone, but also showed that the kidney was not infected and was functioning as well as its fellow, I felt justified in countenancing the delay, leaving him in the hands of his brother, a physician. The next news I had of the case was three months later a telephone message at 1 A.M., stating that after a colic of five days' duration he had ceased to urinate. I found him delirious, febrile and anuric. Incision of the loin revealed an impacted stone, a ureter so gangrenous that it ruptured as I picked it up and a large perirenal collection of urine and pus. I ventured to do a nephrectomy and the patient was fortunate enough to recover though he lay desperately septic for many weeks and did not leave the hospital for three months. In the five years since operation he has passed a stone from his remaining kidney, and he is now suffering from chronic nephritis and high blood-pressure.

In this connection it may be worthy of note that the ureter may be obstructed by crystals, there being no actual stone formation. The type of renal colic that follows a good dinner and a shower of crystals is doubtless not unfamiliar to you. I once cured a renal colic by liberating a bunch of such crystals jammed in the ureter, through poking them with a ureteral catheter. One of my patients got into a much tighter place, as follows:

Case V.—A pale, thin boy, aged seven years, had long been subject to renal attacks (not recognized as such) characterized by fever and vomiting. These attacks were usually relieved by calomel. On the morning of October 23, 1913, he passed some urine containing grit, and thereafter ceased urinating for four days, at which time he came into my hands with bilateral loin tenderness

but no pain, considerable abdominal distention, a pulse of 100, blood-pressure 140, temperature about 100°. I opened both of the pelves of his kidneys and decapsulated the kidneys in twenty-five minutes. The urine was under great tension and was muddy with urate crystals, but no stone was found. The pelves were flushed out and left open. After two weeks of tardy convalescence his loins healed, though ten days later the left one reopened for three days. Roentgen rays were negative after the operation.

Since that time his mother has been a little more prompt in giving him calomel. The urine remained purulent for two years and he still has a trace of albumin, but no casts and no pus, seven years after his operation.

I have searched the records of some 200 cases of renal pain due to stones in an effort to find how long it is possible for a stone to remain in the ureter and still pass without permanent damage to the kidney. Inasmuch as six months appears to be the accepted limit for awaiting the passage of stone after a renal colic, I have enumerated only those that went longer than this without gravely impairing renal function, as follows:

	Cases.
9 to 12 months	5
12 to 18 "	3
18 to 26 "	6

These facts are recorded for edification, not as a guide to practice. They illustrate the extremes, neither of which may be our guide.

Doubtless we may agree that operation for ureteral stone should be advised under three conditions, viz.:

1. Because of the alarming symptoms excited by the stone.
2. Because the stone does not progress and cannot be made to progress by manipulation.
3. Because the stone is more than 0.5 cm. in diameter.

Or perhaps these three reasons might be summarized by the statement that the shape of a ureteral stone determines its fate.

The rounded stone, largely composed of urates or phosphates, produces relatively mild colic and its passage may be awaited with some complacency if it engages in the ureter before it reaches a diameter of 1 cm. But any one who has enjoyed the passage down the ureter of a jagged flake of oxalate crystals so small as to be almost invisible to the roentgen ray will agree that words fail to do justice to the discrepancy between the size of the enemy and the distress it can cause. One can usually judge the shape of the stone with a certain degree of accuracy by the shadow it casts and the depth of the scratch it produces upon the wax bulb. Exceptionally, however, stones escape diagnosis not only by the roentgen rays but by the wax bulb as well. I have three times failed to identify a small stone in the ureter by the wax bulb. One of the cases is so deplorable that it is worthy of contemplation.

CASE VI.—The patient came from out of town for a diagnosis. He had suffered from pain of moderate severity in the right side for three months. The pain suggested renal colic and was accompanied by the passage of blood, either microscopic in quantity or just sufficient to make the urine smoky. When he reached New York his pain had ceased and his urine showed nothing abnormal beyond a trace of albumin and a few leukocytes and red cells. Physical examination revealed nothing wrong. Ureter catheters obtained urine equal in quantity and quality from the two kidneys. Wax bulbs showed no scratch although the catheters went readily to the kidney pelves. A pyelogram was negative. So I sent him home with the statement that he had doubtless passed a small stone without noting its passage from the bladder (this often occurs). Within a week he was back with smoky urine and a little pain. Instead of reëxamining him, as I should have done, I performed the operation that never succeeds in my hands—exploration of the kidney for a diagnosis. On finding the organ normal I even split it from end to end (an operation I had performed but once before and which I believe I may safely promise never to repeat). Result: Zero. I passed a catheter down the ureter to the bladder. This revealed nothing. So I sewed up his kidney no wiser than I had been. He became infected and septic. Pneumonia followed, then empyema. Finally, as he was recovering, he passed a small ureteral stone—and I got the idea.

He has remained well for three years now, and, I am proud to state, considers me a wonderful surgeon who saved his life.

In such a case as this nothing can save the diagnosis except an unfailing clinical conviction that in the face of symptoms suggestive of renal stone no negative evidence is worth consideration. I wonder how many of the cases of renal pain or bleeding that are relieved by a negative exploration of the loin are not actually cases of small ureteral stone undiagnosticated.

But this difficulty of diagnosis applies only to the smallest stones. The others will show, will scratch, will give secondary changes such as dilatation discoverable by pyelography and ureterography, deficient renal function, infection. Indeed a proper diagnosis covers all of these points and ensures their correspondence. One cannot too often remind one's self that the complete clinical picture must include not only a set of statements from the patient, all of which point to the same diagnosis, but a contributory set of data elicited by the more specialized methods of diagnosis. I know no case better calculated to offset the one last related, in which an unwarranted exploration of the kidney almost resulted in the patient's death, as the following, in which the reluctance to exhaust every means of diagnosis, including a surgical exploration, combined with a lapse of clinical acumen to prevent a diagnosis that might have saved the patient's life.

Case VII.—This patient had as his only symptom infrequent hematuria of such severity as to suggest neoplasm. The roentgen rays showed a shadow suggestive of a large stone impacted in the ureter at the brim of the pelvis. This was, alas, before I was using the wax bulb, and cystoscopy and ureter catheterization revealed nothing abnormal. No renal deficiency; no pus or bacteria; no impediment to the passage of the ureter catheter. I should have known that he did not have a stone in his ureter, but I did not. I operated and removed an enterolith from the much dilated vermiform appendix, which was sunk in an adherent coil of small intestine with which it communicated by many openings. I solaced myself with the possession of an interesting specimen and the fatuous theory that this stone might have caused the hematuria.

The patient disappeared for three years and then returned, stating that his hemorrhages had recurred from time to time, latterly with such severity as to cause clotting in the bladder. He had suffered some discomfort in his right loin, but I could not palpate his kidney, and ureter catheterization and roentgen rays were again negative, the right kidney showing plainly and being apparently normal in function, size and shape. As three years had elapsed since the beginning of his bleeding I relinquished the theory of neoplasm which was obviously suggested and once again dismissed him undiagnosticated.

This time he returned in a year, emaciated, his loin full of neoplasm, inoperable to the extent that he died of my effort to remove the kidney which lay upon a bed of carcinomatous glands as big as itself.

May the recital of these woes prove as profitable to you as I believe they have been to me.

Bilateral Stone and the Single Kidney. The problem of stone in the kidney that is supporting the patient's life appears under various forms. We may enumerate the following:

Stone on one side and renal insufficiency on the other:
- Due to stone (*i. e.*, bilateral stone).
- Due to other diseases of the kidney.
- Due to congenital deficiency.
- Due to urethral retention.

Stone in a single kidney:
- Atrophy of the opposite kidney due to disease.
- After removal of the opposite kidney.
- Fused kidney.
- Non-development of the opposite kidney.

This great variety of conditions from stone in both kidneys to stone in the one kidney the patient possesses, presents the common problem of the influence of disease or absence of the opposite kidney upon the treatment of renal and ureteral stone.

Bilateral Stone. This type condition of bilateral surgical renal disease may exhibit various degrees of unilateral or bilateral renal deficiency, but its most interesting phase is that in which the patient complains of unilateral symptoms and examination reveals gravely deficient renal function due to large or multiple silent stone in the opposite kidney. Under such conditions the following rules for operation are doubtless generally acceptable:

1. The kidney showing the better function should be operated upon first.

2. The kidney showing acute symptoms is usually the sounder organ.

3. Impaction of stone in the ureter of the sounder kidney may temporarily reduce its function below that of its fellow. Under such conditions it is safer to operate first upon the side with ureteral stone.

4. Simultaneous bilateral operation may be attempted if the patient's condition is relatively good and the first operation not unduly long (thirty minutes).

5. In an emergency, such as anuria, the sole object of operation should be to provide drainage to the kidney, usually by pyelotomy (which in case of anuria should always be bilateral). Such stones as cannot be rapidly reached and readily removed should be dealt with at subsequent operation.

6. Geraghty's formula, *i. e.*, good concentration of urea and of phenolsulphonephthalein and a small quantity of urine (with consequent low total 'phthalein) may be depended upon to indicate an atrophied or congenitally small kidney inadequate to support life. I have twice correctly diagnosticated unilateral renal deficiency of this nature by the Geraghty formula. My impression has been that bilateral renal stone is very common. I have been surprised to find how few are identifiable among my cases.

I have classified as follows the cases in which the data were sufficient to permit of accurate classification:

Total cases	187
Bilateral	49
Total kidneys involved	236

The calculous crop from these kidneys was distributed as follows (estimates are per kidney, not per stone. Thus if a kidney gets rid of four stones and retains one, only the retention counts):

Stone retained in the pelvis of the kidney	95
Stone permanently arrested in the ureter	60
Arrested in the bladder	21
Arrested in the urethra	3
Stone passed	68
	247

The duplications were as follows:

Pelvis of the kidney and bladder	8
Pelvis of the kidney and ureter (same side)	3
	11

Many of these data run contrary to my preconceptions. Are not more than 25 per cent. of stone bilateral? Are not more than 4 per cent. of calculi arrested in both bladder and kidney pelvis? If 60 stones were arrested in the ureter, did not more than 68 kidneys succeed in passing all their stones? Is it true of stone-bearing kidneys that one-third of them retain at least one of their stones, that one-quarter more do not get all of their stones down the ureter, that from 10 per cent. the stones are retained in bladder or urethra and that only a little over a quarter pass all the stones they make?

But one of the most interesting problems in prognosis these figures do not even hint at. We see most of these cases after they have had a renal colic. Our clinical resources permit us to say with a fair degree of accuracy that a patient who has had a renal colic is or is not free from stone. If he is can we guarantee him against another renal colic? Obviously not. We can do nothing except to treat infection if such exists. Well then if he may have other colics are they going to threaten him more than the first one? My records only answer by failing to show a case where a kidney that passed its first stone successfully, failed to pass the subsequent ones as well. Can this be the general rule? I hope so. At least I am encouraged to tell my patients and myself that a renal colic successfully weathered is the best possible insurance against retention of stone. It means that the kidney drains well, lets its stones escape early.

Silent Stone. My list of silent renal stone cases is the following:

	Cases.
Unilateral silent stone	9
Bilateral silent stone	2
Silent on one side, symptoms on the other	11
	22

The following cases illustrate extremes in the histories of silent stones:

Case VIII.—An indolent, wealthy, heavy drinker. At fourteen years of age he passed a stone after a colic. At fifty he was found to have pyelitis. At fifty-five he began to suffer from neuralgia of the thighs, doubtless due to renal insufficiency. At fifty-eight he began to have mild attacks of hematuria. These continued until at the age of sixty-three he had a severe one, lasting several months. He lost twenty-five pounds in a year and came to me for a diagnosis. The roentgen rays showed his kidneys to be widely distended with stones and one small one stuck at the upper end of the right ureter. After five months of bleeding he passed this stone, regained most of his weight and is now surprisingly active at the age of sixty-seven.

Case IX.—A Russian Hebrew. At eight years of age he had a hematuria. At fourteen he passed a stone. At nineteen litho-

lapaxy (in Russia). At twenty-four he entered Bellevue Hospital septic and with his first renal colic. He passed his stone and I removed large stones from both kidneys simultaneously. He was comparatively well, but with a mild infection of both kidneys when I last saw him six months later.

CASE X.—Entered hospital with as alarming a renal colic as I have ever witnessed. The temperature on admission was 105°. The right loin was intensely sensitive and rigid. Roentgen rays showed the left kidney full of stones, but nothing on the right side. Within twenty-four hours the temperature fell to normal, but the right kidney remained so large and tender that the initial diagnosis of perinephritic abscess was adhered to by certain members of the staff. Meanwhile he was cystoscoped, the left renal deficiency confirmed and a small stone was seen in his bladder. This had evidently caused the right renal colic. He was kept in the ward two weeks while the congestion of the right kidney subsided, after which I successfully removed the left one, finding it completely destroyed by calculi. The stone seen at the first cystoscopy passed painlessly from the bladder and was lost.

CASE XI.—A sedentary business man; rather stout. At eight years of age he had a stone removed from the bladder. He recognized no further symptoms of urinary disease until, at the age of forty-seven, while playing golf, he did one of those things that to the non-golfer are mystery—sprained his back so badly that he had to give up his game. By the time he got home his loin was both swollen and tender. A few days later a physician opened it, letting out a large quantity of fluid blood. After this he was comfortable and able to resume his work, but the incision did not heal and after a while it was discovered that the slight discharge from it contained urine. Roentgen rays showed a kidney full of stones. He refused operation, and three years later he writes me that he still has his little fistula but is otherwise entirely well.

The symptoms of calculous anuria are familiar, as are those of rupture of the pelvis of the kidney. I have operated upon each four times. Two of the anuria cases died, the others recovered, as did all four rupture cases.

The common feature of silent stone cases is that their silence is an ominous one. Whether in kidney, or bladder, the more prolonged the silence the more impairment of renal function has resulted and the greater the danger from any operation.

On the other hand the removal of small silent stones is indicated as a prophylaxis of the very renal impairment that results from their neglect. Such stones as may be removed without tearing of the renal substances should be operated upon after they have reached 2 cm. in diameter.

Stone in a Single Kidney. Let us extend the term "single kidney" to its widest physiologic limit and include not only those cases in which the opposite kidney is anatomically absent but also those in which it is merely physiologically incompetent to support life. May we not conclude that such a condition constitutes a surgical emergency? If the stone is impacted in the ureter of a single kidney it immediately and obviously threatens life; if silent the threat is less immediate, but none the less obvious. Stone in a single kidney not only may but must be operated upon, unless there is some other contra-indication to operation.

I have operated upon several such cases, the result of operation depending more than anything else on the degree of chronic renal deficiency due to prolonged suppuration. My most interesting and brilliant case was the following:

Case XII.—An able-bodied Irish laborer, whose previous history contained nothing relating to his urinary organs, sat for two hours on a board covered with ice, in February, 1915. Within a few hours he had a severe pain in his left loin, and the next day did not urinate. Alarmed at this he consulted a physician, who passed a catheter but obtained no urine. Meanwhile the pain had disappeared and the patient felt perfectly well. So for six days he did nothing, though during that time he passed not a single drop of urine. He then entered St. Vincent's Hospital.

He said he felt well but he was mentally a little stupid, his superficial capillaries a little congested, his intestines distended, his blood-pressure 170, his temperature normal, his left loin slightly tender, but owing to distention the kidney could not be felt.

The roentgen rays showed a large left kidney but no stone. The cystoscope showed a congestion of the bladder vessels corresponding to the skin congestion. There was not a drop of urine in the bladder. The ureter catheter went 30 cm. up the left ureter, but drew no urine. A filiform ureteral bougie entered the right ureter for only 5 cm. and drew no urine.

I therefore immediately cut down upon the right loin but found no kidney there. I turned him over and opened the left loin and found the left kidney very large, congested and tense. I incised the cortex and pushed a tube into the pelvis of the kidney, liberating an ounce or more of urine.

For two days he was semicomatose and then recovered and made a brilliant operative recovery. For three weeks he passed large amounts of urine daily from the loin tube but none from the bladder. From the bladder washings streptococci were obtained. A second cystoscopy revealed nothing new. Then he began to urinate as much as 700 c.c. in twelve hours. I therefore removed the tube and in a week the sinus closed, whereupon the temperature went to 105° and the loin reopened, so I replaced the tube and left it in.

In July, five months after the first operation, he returned to the hospital, still passing all the urine through the left loin. I reopened the loin, found the kidney very adherent and the sinus entering the center of the cortex. I mobilized the lower pole subcapsularly, disclosed the adherent pelvis and the ureter moderately dilated below a narrow tight stricture at the ureteropelvic junction. I opened the ureter and found that I could not pass even a probe through the stricture. I hoped to do a plastic operation, but found that I could not mobilize the ureter or the kidney sufficiently to do so. I therefore made another incision an inch down the ureter and introduced a 20 F. catheter through this up into the pelvis of the kidney, thus splinting the stricture wide open. This tube was left in for three days. Thereafter most of the urine came from the urethra, but four days later his temperature rose to 104° nad remained thereabouts for three days, when he passed a small phosphatic stone. His loin then promptly healed and his convalescence thereafter was uneventful.

Two years later, in July, 1917, after a week of pain and fever in the left loin, he returned. I watched him for ten days, during which he had irregular fever, each relapse of temperature being accompanied by pain in the loin and definite anuria, the longest period of anuria being twenty-four hours. Roentgen rays showed three shadows in the region of the left kidney, two of them regarded as stones. I opened the loin for the third time, found the kidney so bound down that I could hardly budge it, opened it through the old nephrotomy wound and found but one stone, stuck in the orifice of the perfectly patent ureter. The convalescence was entirely uneventful except that I had to irrigate the pelvis of the kidney once through a ureter catheter to reëstablish ureteral drainage.

In 1921, five years after his first operation, he remained entirely well, at work and weighing 200 pounds, but I have had no opportunity to make any examination, except to look at his urine, which showed no pus to the eye.

Infection and Stone. One may well admit the many difficulties that surround the complete cure of the infection so often associated with renal and ureteral stone. A Bacillus coli infection we look upon with a philosophic calm. It is at least not likely to occasion a relapse of the stone. But the cocci do occasion relapse even in kidneys that are seemingly draining well. Fortunately the cocci are particularly vulnerable to antisepsis by hexamethylenamin.

In this connection it may be stated that the frequent occurrence of epididymitis as a complication of renal stone with cocci infection is not without clinical significance. It means at least that the internal genitals are infected. One will of course find pus in the prostate and vesicles. I have taken this hint and in several cases succeeded in clearing up an otherwise intractable postoperative coccic infection by combining urinary antisepsis and massage of the

internal genitals. Lavage of the renal pelvis, on the other hand, has given me no better results than might be expected from the catheterization.

In short the following routine may summarize my views on the treatment of renal infections associated with stone.

1. In operating maul and tear the kidney as little as possible.
2. Assure drainage by dilating ureter strictures widely, and if it seems wise, by fixing the kidney high in the loin.
3. Symptoms suggesting renal retention occurring while the loin fistula is still open call for immediate irrigation of the kidney pelvis through the ureter catheter.
4. During convalescence, hexamethylenamin and bladder irrigation as a routine.
5. The source of infection may be in the tonsils, teeth, bowel, etc., and an effort should be made to get rid of it.
6. The prostate should not be forgotten.
7. Use the wax bulb as a routine to detect the presence of stone or stricture of the ureter even when one does not expect to encounter them.

Operative Statistics. I have performed eighty operations for stone in the kidney pelvis and ureter. They may be classified as follows:

NEPHROTOMY.

24 cases (1 bilateral).

12 cases, of which 4 were known to remain well one to two years after operation.

10 incomplete or relapsed, of which 1 cured by second nephrotomy six years later.

2 cured by secondary nephrectomy.

1 died after secondary nephrectomy.

2 died—1 by renal insufficiency and 1 by sepsis.

NEPHRECTOMY.

33 cases, 22 recovered.

11 died, of which 2 were from pulmonary tuberculosis, the kidney being tuberculous as well as calculous; 2 septic, the opposite kidney being apparently sound at the time of operation; one of these was a secondary nephrectomy. In both the patient was gravely septic at the time of operation.

1 post-operative ileus.

1 uremic, from chronic parenchymatous nephritis.

2 septic (bilateral stone).

3 of renal insufficiency (bilateral stone).

PYELOTOMY.

13 cases (3 bilateral); 1 died, 3 remained severely infected, 1 stone relapsed, 10 cured, and in 8 cases the cures persisted for three years or more.

URETEROTOMY.

17 cases. No deaths. In 3 no stone was found. In 2 of these the stone was subsequently passed, one required subsequent nephrectomy for a cure. 2 relapsed.

Negative exploration of loin for stone—3 cases. All recovered.

The conclusions that may be drawn from this series of cases are the following:

Pyelotomy for the removal of small stones in the renal pelvis is an operation with singularly small mortality, and almost a certainty of cure.

Ureterotomy is equally benign. There is a small prospect of relapse, due to stricture of the ureter, which may be minimized by the routine dilatation of the stricture at the point of impaction. But small stones may elude the operator, and large ones call for nephrectomy, the kidney being destroyed.

Nephrotomy is required for the removal of large or multiple stones in the kidney pelvis. Such cases are almost always infected, and though the mortality is not high the trauma to the kidney parenchyma may excite acute focal suppuration, requiring immediate nephrectomy, and may leave the kidney fistulous or severely infected.

Nephrectomy for stone is always a grave operation; but if the opposite kidney is sound and the stones so large or so distributed that they cannot be removed by pyelotomy, nephrectomy is a safer operation than nephrotomy. This immediate safety is, however, balanced in the long run by the loss of the kidney, since stone is likely to form in the remaining kidney.

Stone or infection of the opposite kidney is thus no contra-indication to ureterotomy or pyelotomy; indeed, it is rather an indication for these operations. But it adds immeasurably to the probability of sepsis from nephrotomy and gives a high mortality from sepsis and renal insufficiency following nephrectomy. Hence while we may well continue to operate upon such cases, forced to it by circumstances or moved by the proper surgical ambition to hope for better results by a fuller appreciation of the meaning of renal function tests and by improvement to operative technic, we may do so only under the most favorable circumstances and with a due appreciation that silent renal stone is often compatible with years of life in relative comfort.

EXPERIMENTAL STUDIES IN DIABETES:
SERIES II. THE INTERNAL PANCREATIC FUNCTION IN RELATION TO BODY MASS AND METABOLISM.

IV. PANCREATIC CACHEXIA.

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Notice of the subject of cachexia is necessary in connection with this series of papers, particularly with a view to the possible criticism that undernutrition treatment represents merely a suppression of glycosuria by cachexia, which may mask the diabetic condition without benefiting it. For the sake of unity other aspects of cachexia must be included in the same paper. They add further to the similarity between clinical and experimental diabetes and thus strengthen the application of results gained with the one form to the other. The marked and rapidly fatal cachexia of totally depancreatized dogs, and their deficiency of wound-healing power and liability to infection, have been known from the time of Minkowski. Attention was previously given[1] to Hedon's "diabetes without glycosuria" and to cachectic disorders in partially depancreatized dogs with or without glycosuria. The present observations will be discussed under the following headings:

Acute deaths following operation.
Subacute and chronic pancreatic intoxication.
Diabetic asthenia.
"Gangrene."
Collapse and prostration as related to glycosuria.
Prolonged cachexia.

ACUTE DEATHS FOLLOWING OPERATION.

Deaths from infection occur sometimes, evidently due in part to diabetic lowering of resistance. Clean surgery prevents peritonitis even after total pancreatectomy, until after some days pus may burrow through all the suture lines. Young diabetic animals are as subject to distemper as human patients to tuberculosis.

The highest non-infectious mortality occurs in senile, obese dogs, generally within one to three days after operation, with an extreme and progressive prostration, generally without glycosuria or acidosis. Dogs in advanced senility without obesity ordinarily pass through

[1] Allen, F. M.: Studies Concerning Glycosuria and Diabetes, 1913, chapter x.

such operations safely. Likewise young obese dogs generally survive the operation easily, though when the obesity is extreme and there is much trauma of the pancreas remnant death may occur from the so-called "fat necrosis." At corresponding intervals after operation, examination of the animals which survive with those which succumb shows no perceptible difference in the changes either in and about the pancreas remnant or in the fat elsewhere. It can only be supposed that senility lowers the resistance to the toxic action of the pancreatic juice.

Pregnant animals, regardless of their nutritive state, are known to be highly susceptible to pancreas operations, which are generally followed by abortion and death within one to several days, though various other abdominal operations may be borne safely. As the fatal result is sometimes so early, it is difficult to ascribe it always to septicemia or other secondary consequences of the abortion, and a special susceptibility of the pregnant animal to pancreatic poisoning seems probable.

Prophylaxis of the fatalities in both obese and pregnant dogs has been attempted by two methods, namely, by preliminary intraperitoneal injections of watery extract of dog pancreas and by preparatory removal of small portions of pancreas. The benefit of either method was doubtful. A very old and fat dog sometimes dies from the quick removal of a small fraction of the pancreas. During the period of injections or successive operations the animal sometimes loses considerable weight, and a diminished susceptibility may be thus explainable. A few successful results were obtained with preparation by either method, but a few were also obtained without preparation.

The above statements are based upon a large series of observations, most of which are included in preceding or subsequent papers. For the sake of brevity it has seemed best to omit individual protocols in this place.

SUBACUTE AND CHRONIC PANCREATIC INTOXICATION.

After the usual partial pancreatectomy, which leaves a remnant communicating with its duct, dogs are sometimes more or less depressed and unwell for several days, and lose weight rapidly, partly on account of indigestion and diarrhea. Swelling and inflammation are generally evident in the pancreas remnant during this period. Still greater decline of weight and strength are commonly found when a portion of pancreas is left isolated from its duct, either in the peritoneal cavity or under the skin. The disturbances are generally transitory, continuing a few days or weeks according to circumstances. They are evidently due to toxic products of pancreatic tissue which is inflamed or undergoing absorption. The early wasting and other symptoms are therefore not attributable

entirely to the diabetes, and care should be used in the interpretation of any metabolic observations during this period. Later under suitable conditions the animals are able to digest reasonably well, gain weight and behave normally except for their diabetic tendency, and then are reliable test objects for metabolic study.

DIABETIC ASTHENIA.

If a totally depancreatized, a partially depancreatized and a phlorizinized dog lose equal quantities of sugar in a given time, the totally depancreatized animal will ordinarily show weakness and depression out of all proportion to the other two, and will die while the others are still strong. Even if the totally depancreatized animal appears lively a test with running reveals his lack of strength. The asthenia of partially depancreatized dogs generally appears late in the period of advanced emaciation. Exceptional partially depancreatized animals show early asthenia and rapid progress to death, almost equal to the consequences of total pancreatectomy. These results seem to be classifiable under three headings: (*a*) Small size of remnant; (*b*) inflammation in remnant; (*c*) unknown causes.

(*a*) Small size of remnant.

Occasional dogs with very small pancreas remnants are strong and long-lived. An example previously published[2] was dog 19, which had only about one-fifty-fourth of the pancreas, and died in an operation two and a half months later, having been very vigorous for a severely diabetic animal in the meantime. As a rule, animals with very small remnants suffer not only from poor digestion but also from a more rapid decline than can be accounted for by indigestion. Some instances of exceptionally rapid decline are the following:

Dog B2–64.

Male, bulldog mongrel; brindle; age five or six years; medium flesh; weight, 14.7 kilos. May 25, 1914, removal of pancreatic tissue weighing 26.5 gm. Remnant about main duct estimated at 1.35 gm. ($\frac{1}{20}$ to $\frac{1}{21}$). Glycosuria was checked by intermittent fasting and meat feeding, so as to be absent part of the time and never above 1 per cent. (2.6 to 12.8 gm. daily output). Nevertheless, the asthenia was out of proportion to the loss of weight, and exceeded that of other fasting partially depancreatized diabetic dogs. June 15, at a weight of 9.6 kilos, 0.2 gm. of pancreatic tissue was removed for examination. June 20 the dog was sacrificed when moribund. The pancreas remnant weighed 1.1 gm., and the autopsy otherwise was negative. Microscopically, the tissue on June 15

[2] (Ibid.), pp. 480, 962.

was normal except for marked vacuolation of islands, while that on June 20 showed recent inflammation in addition.

Though life was not extremely short, the noticeable feature was the disproportionate cachexia in comparison with the glycosuria.

Dog D4–75.

Male; bull terrior mongrel; brindle, aged four or five years; slightly thin; weight, 13 kilos. January 19, 1917, removal of pancreatic tissue weighing 35.3 gm. Remnant about main duct estimated at 2 gm. ($\frac{1}{18}$ to $\frac{1}{19}$). The rapidity of decline and the deficiency of healing of the abdominal wound resembled total pancreatectomy. On January 26 the dog was very weak and was killed. The general autopsy was negative grossly and microscopically. The pancreas remnant was swollen and weighed 5.9 gm. Microscopically there was extreme inflammation; the acini stained irregularly and were in various stages of involution and repair; islands were scarce and small and showed early vacuolation.

In this animal the two factors, small size and inflammation of remnant, were evidently combined.

Cats are more subject than dogs to this form of cachexia. They become diabetic with remnants between one-fourth and one-fifth of the pancreas, and when the remnant is much smaller there is cachexia resembling that of total pancreatectomy.

Cat A1–80.

Female; maltese; young adult; slightly thin; weight, $2\frac{3}{4}$ kilos. November 13, 1913, removal of pancreatic tissue weighing 5.4 gm. Remnant about main duct estimated at 0.4 gm. ($\frac{1}{14}$ to $\frac{1}{15}$). The animal showed characteristic depression, weakness and poor wound healing, without peritoneal infection, and refused all food. The urine record was as follows:

Date.	Volume, c.c.	Glucose, per cent.
November 13	60	0
14	100	2.8
15	90	3.8
16	40	3.3
17	80	6.0
18	80	2.7
19	65	2.8
20	50	2.9
21	35	3.1
22	40	4.0

Death occurred November 22, at a weight of 1800 gm. The urine recorded is that found in the bladder at autopsy. In contrast to the emaciation of trunk and limbs there was a surprising quantity of omental and peritoneal fat. The pancreas remnant was swollen

and hard and weighed 1.5 gm. Microscopically it showed much inflammation and fibrosis, together with the usual diabetic vacuolation of islands. The other viscera were normal grossly and microscopically, except for slight fattiness of the liver and the Armanni vacuolation of renal tubules.

Cat A1–81.

Female; young adult; gray striped; good condition; weight, 3 kilos. November 14, 1913, removal of pancreatic tissue weighing 8.3 gm. Remnant about main duct estimated at 0.4 gm. ($\frac{1}{21}$ to $\frac{1}{22}$). The animal ate about 25 gm. meat on November 16 and 17. Otherwise the clinical course was characterized by refusal of food, profound asthenia and rapid decline, with the following urine record:

Date.	Volume, c.c.	Glucose, per cent.
November 14	20	0
15	75	1.5
16	50	3.6
17	50	7.1
18	80	2.5
19	70	1.6
20	60	0.7

The cat was found dying on the morning of November 21 and was killed. The weight was 2 kilos. The liver was very large and fatty, the other viscera normal. The pancreas remnant, normal in appearance and consistency, weighed 0.6 gm. Microscopically it showed fibrosis, chiefly of interlobular type. The acini were in all stages of fulness, emptiness and involution. Islands were almost impossible to find in a series of eight slides containing four sections each. One definite one was found in the last stages of hydropic exhaustion. The others were apparently reduced to small clumps of alpha cells, the identity of which could sometimes be suspected but not clearly demonstrated amid the inflammation. The process of functional exhaustion was thus exceptionally rapid.

(*b*) Inflammation in remnant.

Dog E5–12.

Male; Dalmatian; aged three years; good condition; weight, 16.25 kilos. March 23, 1917, removal of pancreatic tissue weighing 40.5 gm. The attempt was made to leave a remnant small enough to permit diabetes, yet extending the whole length of the uncinate process. The remnant left consisted of the duct and bloodvessels, with a narrow band of accompanying parenchyma. The dog showed slight appetite on the first two days, but was not fed. There

was marked and increasing prostration like that following total pancreatectomy, with the following urine record:

Date.	Volume, c.c.	Glucose, per cent.
March 23	370	Slight
24	146	1.7
25	810	2.9
26	470	1.8
27	468	3.8
28	248	3.3
29	328	2.4

The dog was found dying on the morning of March 30. There was intense inflammation of the pancreas remnant and distinct congestion and edema of the hypophysis, otherwise nothing unusual in the autopsy.

Dogs C3–83 and D4–16.

Dog C3–83 became diabetic after removal of five-sixths of the pancreas on April 20, 1916, and dog D4–16 after removal of $\frac{11}{12}$ of the pancreas on the following July 14. The two animals were used for parallel experiments, involving similar glycosuria and other conditions. The contrast in the strength of the two was striking throughout. Dog D4–16 died August 23 while the other dog was still vigorous. The protocols are not given in detail because nothing could prove that some extraneous factor was not the cause of the difference. The number of such observations furnishes evidence that the peculiarity is not accidental. One noteworthy feature in the present instance is the hypertrophy of the pancreas remnant of Dog D4–16, which was estimated at 4.4 gm. at operation and found to weigh 8.2 gm. at autopsy. It thus weighed actually more than the remnant of dog C3–83, which did not hypertrophy. It consisted of normal appearing acinar tissue without fibrosis, with varying numbers of islands. The digestive power should therefore have been as good as in dog C3–83. On the other hand, other studies indicate that the hypertrophy is an indication of preceding inflammation.

(*c*) Unknown causes.

Dog E5–26.

Male; Newfoundland; black, aged three years; good condition; weight, 24.1 kilos. April 25, 1917, removal of pancreatic tissue weighing 33.7 gm. Remnant about main duct estimated at 5.7 gm. ($\frac{1}{7}$). Glycosuria was absent until bread was fed on April 27 and thereafter was heavy. The dog maintained good appetite and cheerfulness, and behaved normally except for surprising weakness, such that he could stand or walk only with great effort. On May 6 the diet was changed to 200 gm. suet, which was fed daily until May 14, after which lung was added. The glycosuria rapidly

diminished and was absent after May 11, and strength was regained at a corresponding rate, even on the protein starvation. The animal remained strong thereafter in the aglycosuric condition. Such asthenia in early diabetes and gain of strength on complete fasting are sufficiently familiar in human diabetes, but are rare in dogs. No special cause was found in the later history or autopsy of this animal.

CAT B2–06.

Male; yellow and white; old; very fat; weight, 4.2 kilos. May 12, 1914, removal of pancreatic tissue weighing 8.4 gm. Remnant about main duct estimated at 2.9 gm. ($\frac{1}{4}$). The animal ate well and showed heavy glycosuria on milk and meat feeding. At the same time the weakness was marked and progressive, and death occurred June 1 at a weight of 2.8 kilos. The bladder at autopsy contained 55 c.c. urine, with 1.8 per cent. sugar. Except for the very fatty liver, nothing noteworthy was found in the viscera. The pancreas remnant, normal in appearance and consistency, weighed 1.9 gm. Microscopically there was no inflammation or fibrosis except a trifle at the margins. The acini were normal except for minimal zymogen content, which may explain the small weight of the remnant. Islands were present in fair number but were maximally vacuolated.

Remarks. Asthenia is known as a prominent symptom of diabetes, which occurs in the late stages of diabetes in all patients and animals, along with emaciation and other severe disturbances. It occurs much earlier in some patients, most totally depancreatized dogs and in exceptional partially depancreatized animals. Patients generally regain strength under treatment in proportion to the diet they become able to assimilate, but a few continue to complain of weakness even when free from glycosuria and hyperglycemia on diets which are theoretically adequate. Possible causes of asthenia may be considered as follows:

(*a*) *Loss of Body Fat.* In patients asthenia may be out of proportion to the state of apparent nutrition, may even be present with obesity, and varies between individuals independently of the body weight. Depancreatized dogs, especially if obese before operation, may die while still rich in fat, and at all stages are weaker than normal dogs with a corresponding degree of emaciation.

(*b*) *Loss of Sugar or Nitrogen, or Both.* The above experiments did not include nitrogen analyses, but there is little doubt that phlorizinized dogs, unless they happen to die from acidosis, may far surpass totally depancreatized dogs in strength and in duration of life, while losing even greater quantities of both glucose and nitrogen. Patients sometimes exhibit asthenia when their carbohydrate and nitrogen balance are still fairly favorable, and the great majority

of them gain strength under fasting and reduced diet[3] even though they lose sugar and nitrogen during the process.

(*c*) *Severity of Diabetes.* If the severity of diabetes be judged by the D:N ratio and respiratory quotient, it is known that totally depancreatized dogs do not necessarily exhibit the maximal ratio, especially during fasting; also partially depancreatized dogs in the later stages of their diabetes may show maximal ratios (and presumably corresponding respiratory quotients) while retaining greater strength and liveliness and living much longer than totally depancreatized animals. If severity be judged by lack of island tissue, a resemblance exists between animals which have had the pancreas completely removed, or in which the remnant is of minimal size or damaged by inflammation, or in which all the beta cells have been lost by hydropic degeneration, as in some of the examples given above. But many animals retain fair strength and live for a number of weeks or months after their beta cells are thus lost, while many patients and occasional animals (*cf.* dog E5–26 above) exhibit marked asthenia while the diabetes is still early and mild. In human cases the asthenia is not even a sign of intrinsic severity, for it is complained of in many cases which are benign and easily controllable throughout. Cases with asthenia out of proportion to the apparent nutrition after cessation of glycosuria are generally grave, but not more so than many others in which the strength is longer retained.

(*d*) *Nervous Influence.* A neurotic element may be assumed in many patients, whose nervous systems are specially susceptible to the depression of diabetes. Some differences in this respect may be supposed to exist also between animals, but a more important cause is indicated by the fact that in them the asthenia so often progresses to early death.

(*e*) *Indigestion.* Totally depancreatized dogs and those with very small remnants naturally suffer from impaired digestion and diarrhea. Whether the cause be purely an enzymatic or partly an endocrine deficiency, pancreas feeding in numerous trials in this series has never been able to restore anything like normal digestion. But the differences in strength are found also in fasting animals, and the asthenia of human patients seldom has any relation to digestion.

(*f*) *Intoxication.* In some animals absorption of pancreatic poisons may play a part, but this is obviously not the case after total pancreatectomy, and it is seldom to be suspected as a cause of the asthenia of human patients. Acidosis is accompanied by a similar and very profound weakness in both patients and animals, but this factor was excluded in the animal experiments, and the type of asthenia in question is often found in patients without acidosis.

[3] Ergometric tests in patients were made by J. R. Williams, Arch. Int. Med., 1917, xx, 399–408.

Toxemia of intestinal or unknown origin is assumed by some writers in connection with human diabetes, but there is no reason why totally or partially depancreatized dogs, especially if fasting, should suffer from intestinal intoxication, and the assumption of unknown toxins merely cloaks ignorance and confuses the problem unless some proof of their existence is produced.

(*g*) *Endocrine Deficiency.* Asthenia is a fairly common symptom of endocrine deficiency, even in cases which involve no impairment of nutrition in the ordinary sense. Addison's disease and some hypophyseal disorders are familiar examples. The most probable theory of diabetic asthenia, aside from the part which is explainable by impaired food assimilation, is that it is an effect of the lack of pancreatic hormone either upon the body cells directly or upon other organs of internal secretion. It would thus be easily comprehensible that this effect might differ somewhat with differences of individual constitution.

"GANGRENE."

A similarity has long been recognized between the gangrene of human cases and the deficiency of wound-healing in totally depancreatized dogs. The dry gangrene which is the commonest clinical form arises always on a basis of arteriosclerosis, and as dogs seem to be not subject to arteriosclerosis, they do not exhibit this form of gangrene. The other form of so-called gangrene, consisting in superficial infections and ulcers which spread instead of healing, occurs in only a small minority of either dogs or patients, and about as frequently in one as in the other. Mention was made in Series I[4] of dog B2–56, which showed unusually rapid downward progress and cachexia. With this there was a development of trophic ulcers as marked as in any human case. One of these perforated into the right elbow-joint and gave rise to a large abscess in the axilla. Other examples are the following:

Dog B2–11.

Female; mongrel; black and white, aged two years; good condition; weight, 6 kilos. November 20, 1913, removal of pancreatic tissue weighing 16.9 gm. Remnant about main duct estimated at 0.6 gm. ($\frac{1}{29}$). Though the remnant was small and the feces accordingly somewhat bulky, the dog showed no more than the usual glycosuria and other symptoms on meat diet. Early in December something caused a trivial abrasion of the right ankle-joint. By December 8 the whole leg was hot and swollen, without any definite sinus leading from the point of abrasion. Incisions released considerable pus but did not stop the spread of the infection. Death occurred with pneumonia December 11, at a weight of 3 kilos.

[4] Jour. Exp. Med., 1920, xxxi, 560 and 594.

Dog B2–46.

Male; mongrel; yellow, aged four years; thin but strong; weight, 23.25 kilos. March 26, 1914, removal of pancreatic tissue weighing 32.5 gm. Remnant about main duct estimated at 5.9 gm. ($\frac{1}{6}$ to $\frac{1}{7}$). Glycosuria remained absent until bread feeding was begun on March 30, and was heavy thereafter (up to 6 per cent. in above 2000 c.c. of urine). The asthenia was more marked than in any of the dogs mentioned above as examples of asthenia, and the susceptibility to "trophic" or progressive ulceration equalled or exceeded that of human cases. Death occurred by hemorrhage on April 13.

Other examples will be omitted for the sake of brevity. Certain facts are available concerning the cause of the abnormal liability to infection and necrosis: (1) It is not due to simple malnutrition, for carbuncles and intractable ulcers occur in obese diabetics who are apparently in nutritive equilibrium, and are much commoner among diabetics than among equally undernourished patients with other diseases; (2) it is known that control of the glycosuria and hyperglycemia is the most important means of preventing or curing these conditions, and for this reason speculation has attributed their cause to direct injury of the excess of sugar by osmotic or other action or to the favoring influence of sugar upon bacterial growth. A previous attempt[5] failed to produce any of the supposed consequences of sugar excess by long-continued injections of glucose or other sugars. In more recent experiments subcutaneous injections of 0.1 gm. phlorizin daily have been found to keep the blood sugar of totally depancreatized dogs at a low level, but their impaired healing power, resistance to infection and other disorders have not been in the least benefited. Furthermore the immense majority of partially depancreatized dogs exhibit healing and resisting power practically identical with the normal, even when their hyperglycemia and glycosuria exceed those of totally depancreatized dogs in both degree and duration. The mere loss of sugar and nitrogen from the body is evidently not responsible, for totally phlorizinized dogs bear operations reasonably well. The factor of dryness of the tissues is also thus controlled, for some phlorizinized or partially depancreatized dogs evidently undergo greater desiccation than the average totally depancreatized dog. (3) The actual endocrine deficiency, in addition to any of the above factors, must be invoked here as in the case of asthenia. The almost uniform difference between totally and partially depancreatized animals is thus explainable, and the special incidence in individual animals or patients may be accounted for by constitutional variations in resistance and the occurrence of predisposing injuries.

Allen, F. M.: Studies Concerning Glycosuria and Diabetes, 1913, chapter iii.

COLLAPSE AND PROSTRATION AS RELATED TO GLYCOSURIA.

Examples were previously given[6] of the prevention of glycosuria by weakness or prostration, and numerous others might be added from the present series. Dog D4–76 underwent operation on January 19, 1917, and died January 22 from necrosis of most of the pancreas remnant. Here the diabetes should have approached that of a totally depancreatized animal, but the principal symptom was prevented by intoxication. The instance is mentioned because of the similarity to some human cases of fulminating pancreatitis. In Series I, reference was made to animals in which glycosuria was stopped and the progress of diabetes halted by distemper or other causes of anorexia and emaciation. Such animals sometimes later enjoyed excellent health and a high food tolerance in consequence of their spontaneous undernutrition treatment. When the diabetes has become established in a sufficiently severe form, it cannot be halted by fasting or any other known means. In the writer's experience totally depancreatized dogs as well as the partially depancreatized ones with the severest diabetes ordinarily die after continuous fasting or any intercurrent illness or accident with heavy glycosuria present to the end. In the monograph (1913) already mentioned, references were made to the literature concerning absence of glycosuria in totally depancreatized animals after such extreme procedures as removal of the liver or adrenals, or high section of the spinal cord. Any therapeutic significance of such results can be imagined only on the basis of two fallacies, one the confusion between glycosuria and diabetes and the other the indefensible doctrine of diabetes as a pure overproduction of sugar. If it be believed that an animal is diabetic because it cannot assimilate carbohydrate without the internal secretion of the pancreas, obviously the removal of some other organ cannot restore the lost power. Likewise the cessation of glycosuria in occasional totally depancreatized animals in the last hours of life has no therapeutic significance. The very fact of total absence of the pancreas renders such animals unfit for therapeutic experiments unless it is a question of some extract or other agent which can replace the pancreatic function. The results of the undernutrition treatment of patients and partially depancreatized animals are significant for both theory and practice because it can be shown that they do not represent a mere suppression of glycosuria by cachexia, but accomplish an actual raising or preservation of the power of food assimilation and permit a long or indefinite continuance of life.

[6] (Ibid.), p. 492.

PROLONGED CACHEXIA.

The following are rare instances in which diabetes seemed to be superseded by some unknown cachectic condition, producing results different from those of simple undernutrition. Cats seem to be more liable than dogs to this abnormality.

CAT A1–91.

Male; gray striped; middle aged; slightly thin; weight 3.1 kilos. January 13, 1914, removal of pancreatic tissue weighing 5.8 gm. Remnant about main duct estimated at 1.8 gm. (about $\frac{1}{4}$). There was glycosuria on milk and meat diet and none on meat alone. The appetite and health seemed excellent. The glycosuria was allowed to continue and increase up to 5 per cent. in 455 c.c. urine on February 6. February 7, at a weight of 3.2 kilos, fasting was begun. The glycosuria immediately fell to traces, rose to a moderate reaction on February 10, then fell and was absent after February 12. February 16, at a weight of 2.6 kilos, feeding was begun with 20 gm. cooked beef-lung, increasing gradually until on February 23, 140 gm. lung and a live mouse were fed. The weight meanwhile had been falling rapidly to 1.8 kilos; the cat retained appetite and appeared well except for remarkable weakness and weariness. Lung, suet and raw pancreas were then fed as abundantly as possible. The digestion seemed rather poor, as indicated by bulky formed feces, but the cachexia was more advanced and progressive than is seen in plain fasting. Death occurred February 26, and no cause could be found at autopsy. The microscopic examination of liver, kidneys, adrenals and thyroid was negative. The pancreas remnant, normal in appearance and consistency, weighed 1.8 gm. It was fully normal microscopically; the acini were well filled with zymogen; islands were abundant and free from vacuolation.

CAT A1–94.

Female, adult; white and black; thin; weight, 2 kilos. January 21, 1914, removal of pancreatic tissue weighing 3.7 gm. Remnant about main duct estimated at 0.8 gm. ($\frac{1}{5}$ to $\frac{1}{6}$). The animal refused food except for a trifle of milk, and the highest glycosuria was 0.5 per cent. in 25 c.c. urine. Death occurred on January 25, with urine sugar-free, at a weight of 1.6 kilos. Autopsy showed no cause. The pancreas remnant weighed 0.6 gm., and was normal in acini and islands.

The history of cat A1–95 was closely similar.

Some atypical results of this character caused the writer formerly[7] to conclude wrongly that cats are unsuitable for diabetic experiments.

[7] (Ibid.), p. 502.

Cat A1–96.

Male; gray and white; large, strong adult; excellent condition; weight, 3.4 kilos. February 9, 1914, removal of pancreatic tissue weighing 5.6 gm. Remnant about main duct estimated at 1.4 gm. ($\frac{1}{5}$). Glycosuria was produced at first only by milk. It was present March 1 to 23 on meat diet, then ceased spontaneously. With addition of milk it was present March 30 to April 9. On this date two tiny fragments of pancreas, with an aggregate weight of 0.15 gm., were removed for microscopic study. Then on fasting, glycosuria was absent after April 11. A diet of beef-lung or liver was begun with 50 gm. on April 13, increased rapidly to 300 gm. and then *ad libitum*. The cat meanwhile rapidly lost weight and strength without glycosuria, and died April 26, at a weight of 1.9 kilos. The autopsy revealed no gross or microscopic cause of the condition. The pancreas remnant weighed 2.25 gm. Microscopically the tissue removed April 9 was normal except for marked vacuolation of islands. At autopsy there was some interlobular fibrosis; the acini were nearly empty but otherwise normal; islands were scarce in some sections, abundant in others, with most of their cells normal but a few showing slight persisting vacuolation.

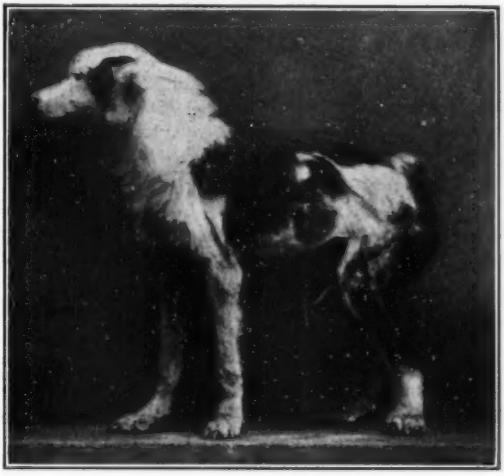
In several dogs glycosuria has been unexpectedly absent or has ceased for unknown cause after it has been present for a longer or shorter time. These instances of cachexia have confirmed the previous conclusions[8] that the duration of life is generally far shorter than in cases in which diabetes develops in typical form. The most marked example of prolonged cachexia was the following:

Dog D4–70.

Male; mongrel; white and black; shaggy; aged four years; medium nutrition; weight, 15.5 kilos. January 10, 1917, removal of pancreatic tissue weighing 31.6 gm. Remnant about main duct estimated at 2.6 gm. (about $\frac{1}{13}$). There was no glycosuria until bread and milk was fed on January 13, causing a slight reaction which disappeared on the same diet. Beginning January 18 a diet of bread and 200 gm. glucose maintained glycosuria until January 23, when it ceased. Thereafter the dog ate the same full pan of bread, with 300 gm. glucose, 200 gm. lung and 100 gm. suet without glycosuria. Beginning January 27, analyses of urine and feces were performed on a diet of 200 gm. lung, 250 gm. bread and 100 gm. suet, which showed only a moderate deficiency of food absorption; also a genuinely high tolerance was demonstrated by an intravenous glucose test and a series of blood sugar analyses, but all these records were lost. February 10, 0.5 gm. phlorizin suspended in oil was

[8] (Ibid.), p. 500.

injected subcutaneously, and heavy glycosuria continued until February 15, indicating a full ability to form and excrete sugar under this stimulus. The weight had mostly remained low, between 13 and 14 kilos, but rose by April 4 to 16.4 kilos. At this weight the feeding of bread and soup *ad libitum* with 100 gm. glucose brought on glycosuria, which ceased promptly when the diet was changed to 400 gm. lung and 200 gm. suet. By May 4 the dog was still lively and happy, with enormous appetite, but was showing hair loss and unsteadiness of legs. Because the symptoms resembled those of fat intoxication (produced in normal dogs by diets too high in fat and low in protein) the diet was changed on May 22 to lung and bread, with milk occasionally, and bonemeal to supply salts. On June 12 and July 27 small portions of pancreas were removed for



microscopic examination without giving rise to glycosuria. The pancreas remnant appeared normal grossly and microscopically. The body weight fell as low as 10.3 kilos, notwithstanding edema, but rose later to 12.5 kilos. Death occurred, apparently from simple weakness, on September 27. The pancreas remnant, slightly firm and nodular, was in free communication with its duct, and weighed 2.9 gm. Microscopically it showed slight fibrosis, interacinar as well as interlobular, but the acini were large and well filled and the islands abundant and normal. Gross and microscopic examination of the other viscera revealed no abnormalities to account for the condition.

The above photograph was taken on July 5. The dog unfortunately was not photographed when normal, but was a rather

handsome animal with long thick hair. The hair loss is seen on the head and ears, trunk, limbs, and the naked end of the tail visible between the legs. Edema without evidences of nephritis is occasionally seen in cachectic dogs, even without pancreas operations. It was greater here in the hind than in the front limbs, and was not like myxedema, but consisted in an accumulation of clear fluid which flowed freely from a needle puncture. The dog remained in excellent spirits throughout. Signs of sexual activity were completely lacking, and the animal was somewhat silly in mentality, as J. H. Pratt has stated[9] concerning young dogs with pancreatic atrophy.

Conclusions. 1. In addition to some acute deaths from unknown causes shortly after partial pancreatectomy, examples were given of diabetic asthenia and diabetic gangrene in animals, which add another detail to the resemblance between clinical and experimental diabetes. Reasons were given for considering both the asthenia and the gangrene as due not to simple malnutrition, hyperglycemia, glycosuria or other causes, but rather to the specific endocrine deficiency.

2. Examples were also given in which the diabetes of dogs and cats was replaced by a fatal cachexia of unknown nature. It is not certain that the condition in all these instances was the same. Malnutrition due to impaired digestion or intestinal absorption was probably one factor, but the results seem to differ in some respects from simple undernutrition, and may possibly bear some relation to the metabolic alterations in states of prostration which suppress glycosuria even after total pancreatectomy.

3. It is highly important to distinguish the mere suppression of glycosuria by some injury, poison or cachexia from genuine control or improvement of the diabetes. It is thus impossible to use totally depancreatized dogs for any therapeutic experiments, unless for testing some agency which is supposed to replace the internal pancreatic function. The results of the undernutrition treatment of animals and patients are distinguished from mere cachectic suppression of glycosuria by the fact that the power of food assimilation is demonstrably strengthened, the general health improved and life lengthened instead of shortened.

[9] Personal communication. Also Jour. Am. Med. Assn., 1912, lix, 322–325.

PULMONARY SEQUELS OF INFLUENZA.

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The vast majority of patients affected with acute epidemic influenza recover and hardly any traces are left behind, as far as can be ascertained by available clinical methods. In a small proportion, after the acute symptoms have subsided, the patients remain with certain pathological changes in the respiratory tract, producing annoying symptoms often confusing to those who attempt to ascertain the real trouble. These chronic symptoms, as well as the pulmonary lesions responsible for them, last for months in many cases, while in some the pathological changes in the lungs and bronchi appear to be so serious that a *restitutio ad integrum* can hardly be expected. During the past two years the number of patients presenting symptoms and signs of chronic disease of the respiratory organs directly traceable to acute epidemic influenza has been quite large. It is the purpose of this paper to offer a brief outline of the pathology, symptomatology, and prognosis of the sequels of influenza in the respiratory tract as encountered by the writer in private and hospital practice.

Chronic influenza was already noted by clinicians after the epidemic of 1890–1891. Thus, R. Pfeiffer[1] speaks of chronic influenzal bronchitis lasting several months after the acute disease had run its course. The symptomatology and course of the trouble as described by Pfeiffer does not materially differ from those recently observed by the writer in New York. Similarly, Finkler,[2] Albert Fraenkel,[3] J. Tessier,[4] Maizon,[5] Collet and Chotin,[6] Egger,[7] and many others, have some twenty-five years ago described in detail certain forms of chronic influenza, and many have emphasized that its differentiation from pulmonary tuberculosis is often very difficult.

Since the epidemic of the past two years several writers in Europe have also described chronic forms of influenza. S. Korach[8] F. Meyer,[9] Ch. Roubier,[10] Feilchenfeld[11] and others have either men-

[1] Die Aetiologie d. Influenza, Ztschr. f. Hyg. u. Inf., 1893, xiii, 357.
[2] Infektion d. Lungen durch Streptokokken u. Influenzabazillen, Bonn, 1895.
[3] Mitt. über influenza, Deutsch. med. Wchnschr., 1894, xx, 49; Spez. Pathol. u. Therap. d. Lungenkrank., Berlin, 1904, pp. 436, 530, 534.
[4] Leçons sur la grippe-influenza, Paris, 1893.
[5] De la grippe chronique a forme tuberculose, Thèse de Lille, 1894.
[6] Deux cas de grippe a forme pseudo-phymique, Lyon médicale, 1894.
[7] Etude clinique des formes pseudo-phymique de la grippe, Thèse de Lyon, 1894–1895.
[8] Zur Pathologie d. Influenza, Berl. klin. Wchnschr., 1919, lvi, 218.
[9] Zur Behandlung d. Grippenpneumonie, Deutsch. med. Wchnschr., 1919, xlv, 173.
[10] Grippe et tuberculose, Lyon méd., 1919, li, 428, 485.
[11] Aus d. Aerztlichen Praxis, Deutsch. med. Wchnschr., 1919, xlv, 439.

tioned it or given compete descriptions of the various clinical forms in which these chronic sequels manifest themselves. J. E. Kayser-Petersen[12] describes tracheobronchial adenitis, at times reactivation of old tuberculous lesions in these glands, as sequels of influenza. Fürbinger[13] speaks of chronic pneumonia without tubercle bacilli in the sputum as frequent sequels. Fraenkel and Krehl[14] emphasize the above views and state that in many cases only repeated examinations of the sputum decides the diagnosis. O. Bossert and B. Leichtentritt,[15] have described chronic pneumonic processes in children as sequels to influenza. Brüggemann[16] gives details of chronic perichondritis of the larynx following epidemic influenza, which is very difficult to differentiate from syphilis and tuberculosis of the throat.

As encountered in the practice of the writer the chronic forms of influenza manifest themselves in various clinical pictures. In a large proportion of cases, especially those in which the primary disease ran a moderately mild course without pulmonary complications, the lesion in the throat lingered on for weeks or even months. In others in whom the bronchi were severely affected during the course of influenza, subacute, purulent bronchitis, general or apical, remained for an indefinite time. In still others in whom the lungs and pleura were implicated during the course of the primary acute disease, bronchiectasis, chronic abscess of the lung, thickened pleura, etc., remained. Many of these patients were pronounced tuberculous and admitted to sanatoriums and hospitals for tuberculous.

Rhinopharyngitis. In a considerable proportion of patients who recover from the acute symptoms of influenza the persisting cough and expectoration are due to a lingering or chronic inflammatory process in the pharynx and tonsils. In some the redness of the fauces remains for weeks and months and they persist in hawking, coughing and expectorating; they remain weak and debilitated; some are completely disabled from pursuing their vocations. Rarely hoarseness is a pronounced symptom, but perichondritis of the larynx, as described by Brüggemann,[16] has not been observed by the writer. Fever is entirely absent in most cases, though instability of the pulse-rate is to be observed. Bradycardia, however, is not rare. In a few slight exertion was instrumental in raising the temperature. Owing to their debility, lack of endurance and cough, they are treated either for neurasthenia or as tuberculosis "suspects." Physical exploration of the chest fails to reveal anything abnormal in the bronchi and lungs. In those in whom certain

[12] München. med. Wchnschr., 1919, lvi, 1261.

[13] Quoted from Petersen, Ibid.

[14] Ibid.

[15] Chronische Lungenkrankungen bei Kindern infolge Influenza, Deutsch. med. Wchnschr., 1919, vol. xlv.

[16] Perichondritis des Kehlkopfes nach Grippe, München. med. Wchnschr., 1919, lxvi, 641.

abnormal findings are elicited by physical exploration of the chest, due in fact to preëxisting disease of the pleura or lung, and which are ordinarily disregarded by careful physicians, a diagnosis of tuberculosis is liable to be made. Several of these cases have been referred to the Montefiore Hospital as tuberculous:

Case I.—I. C., admitted July 20, 1919. An errand boy, aged nineteen years; his father died of pulmonary tuberculosis and he had an attack of pneumonia five years previously. He recovered and felt well until January, 1919, when he was laid up with influenza for a week. He then resumed work, but weakness and debility prevented and he applied to the Department of Health for diagnosis and treatment. He was sent to the Municipal Sanatorium for the Tuberculous and then transferred to another hospital for advanced tuberculosis. Neither institution suited his fancy and he asked to be transferred to the Montefiore Hospital.

On admission he complained of cardiac palpitation, weakness, dyspnea on slight exertion, pains in the chest and loss of weight. A careful physical examination showed no abnormal findings in the lungs and bronchi, excepting some slight impairment of resonance over the right apex. The breath sounds were normal and no adventitious sounds could be elicited. A radiogram of the chest did not show anything abnormal. While at the hospital his temperature, pulse and respiration were normal; the urine was negative. No sputum could be obtained for examination because he did not expectorate, nor did he cough. His fauces showed the characteristic signs of inflammation.

Case II.—F. M., woman, aged thirty-eight years. Family and personal history irrelevant, excepting that in 1912 she "caught cold" and coughed. Physicians diagnosed bronchitis at the time and she was relieved by medication. She felt well until October, 1918, when she contracted influenza and again began to cough. After remaining in bed for about two weeks the fever, etc., disappeared, but she continued to cough, expectorate, felt rather weak and lacked endurance. But her pulse, temperature and respiration remained normal throughout her stay at the hospital. Repeated examinations of the sputum failed to disclose tubercle bacilli, though various cocci were found. On physical examination nothing abnormal could be discovered in the chest outside of slight impairment of resonance over the right apex. The redness of the fauces has been marked. For about nine months, weakness, cough and expectoration have persisted.

These two cases illustrate the rhinopharyngeal form of chronic influenza. We have met with numerous cases of this type during the past two years. It has been our experience that the prognosis

is very good. Sooner or later, in some cases after six to twelve months, strength is regained concurrent with the disappearance of the local inflammatory phenomena in the throat. A rest out of town for a few weeks is perhaps the best mode of treatment.

Purulent Bronchitis of Influenzal Origin. Of greater significance is a persisting inflammatory process in the bronchi with resulting purulent bronchitis, of which we have seen many cases during the past two years. More or less severe cough, profuse expectoration of mucopurulent, rarely purely purulent material, teeming with cocci or influenza bacilli, and debility persist for weeks, at times for months. It is noteworthy, and of diagnostic significance, that despite the extensive catarrh of the bronchi most of these patients have no fever; and the pulse may be normal, at times even bradycardia is observed, and they do not lose in weight; many even gain in weight to a remarkable extent. In several cases I have observed dyspnea on slight exertion, in a few acrocyanosis.

Physical exploration of the chest shows that its resonance remains unimpaired and there are no changes in the breath and voice sounds, but that adventitious sounds of various kinds abound all over the chest, or at least over the lower lobes of the lungs posteriorly. The diagnosis is clear and no suspicion should be entertained that we are dealing with a more serious condition than catarrhal bronchitis. It will be observed that, despite the cough and profuse expectoration of purulent or mucopurulent material, the general condition of the patient hardly suffers; in fact, he may be gaining in weight and may also be able to pursue his occupation, though more or less annoyed by the symptoms. It has been my impression that diffuse purulent bronchitis is more liable to occur in patients who during the attack of influenza had symptoms of general bronchitis; those suffering from complicating bronchopneumonia are left, as a rule, with symptoms and signs of localized bronchitis or bronchiectasis, as will be shown later on. In several cases in which myocarditis was one of the sequels of acute influenza there was found, in addition to the dyspnea, acrocyanosis, tachycardia, etc., a dry form of bronchitis with sibilant and sonorous rales all over the chest.

The diagnosis is arrived at by the method of exclusion. Diffuse purulent bronchitis is usually secondary to cardiac or renal disease, both of which are lacking in the influenzal cases. The fact that the symptoms have appeared with occurrence of acute epidemic influenza, have persisted after the acute attack subsided, that there is no serious effect to be observed on the general nutrition of the patient, and that despite its abundance the sputum lacks tubercle bacilli, should all be considered. The prognosis is good, though in some cases the symptoms are liable to linger for weeks and months. I have cases under my care in which the cough and expectoration have lasted over a year. A short vacation in the country appears to be the best and most effective mode of treatment. Expectorant medi-

cation has no effect on the local lesion, nor on the annoying symptoms; while it is liable to cause gastric derangement.

Apical Catarrh. Some twenty years ago several authors spoke of apical catarrh of influenzal origin, but others maintained that it is almost invariably tuberculous in character. However, during the past two years the number of patients with catarrhal lesions in the upper lobes of the lungs without tubercle bacilli in the sputum has increased enormously. Many of them are being treated as tuberculous; nearly all give a history of epidemic influenza at the onset.

The differentiation between influenzal apical bronchitis and pulmonary tuberculosis is at times very difficult indeed. The writer has been guided by the following points: Its onset with influenza speaks against tuberculosis. The lack of constitutional symptoms of phthisis, especially fever, tachycardia and emaciation, is greatly against tuberculosis, because active phthisis with numerous rales audible over an apex, a slow pulse-rate and normal temperature are exceedingly rare, excepting in far advanced fibroid cases, which are easily diagnosed along other lines. Lack of signs of pulmonary retraction of the affected apex as revealed by topographic percussion, also favors apical catarrh—the resonance above the clavicle remains unimpaired despite the presence of numerous subcrepitant rales and perhaps bronchovesicular breathing; this is hardly ever seen in tuberculous apical lesions. If to these is added the fact that, though abundant, the sputum is negative on several examinations, tuberculosis should be excluded. It may also be added that blood-streaked sputum does not by any means favor the diagnosis of tuberculosis in this class of cases. On the whole it will be noted that these apical sequels of epidemic influenza do not at all impair the general health of the patient. He coughs and expectorates, at times blood-streaked sputum, but he maintains his weight, has a good appetite and gains in weight, although some rales are heard while his chest is auscultated.

Bronchiectasis. Bronchiectasis has heretofore been somewhat of a mysterious disease, especially as to its origin. Some authors have considered it very rare while others stated that they meet with many cases; some said that most cases are due to foreign bodies in the bronchi and urged bronchoscopic treatment (Chevalier Jackson). Many writers have maintained that bronchiectasis originates mostly in influenza. Pfeiffer pointed out that the contents of bronchiectasic cavities are often teeming with influenza bacilli. Osler[17] agreed with this view. He said: "The disease seems to have increased in frequency since the influenza epidemics of the past fifteen years." The writer, dealing in his hospital work with large numbers of Eastern European patients, has met with numerous cases of bron-

[17] Principles and Practice of Medicine, 1916, 8th ed., p. 625.

chiectasis, the history showing that the disease was acquired long before the patients had emigrated to the United States. Among native patients the number with dilated bronchi was much less. This may explain the reason why there is such a divergence of opinion as to the frequency of bronchiectasis. It apparently depends on the character of the clinical material. However, during the past two years, since the pandemics of influenza, large numbers of patients are met who present symptoms and signs of bronchiectasis and who date the origin of their trouble to the epidemic disease. At present bronchiectasis, if for its frequency alone, assumes greater importance from the standpoint of diagnosis, prognosis and treatment than formerly when cases were comparatively scarce, at least among the native population.

The lesion follows bronchopneumonia, pleurisy or both. Small areas of bronchopneumonia of a chronic type occur and excessive growth of connective tissue is effective in contracting and destroying the pulmonary parenchyma; the elasticity of the lung tissue is thus impaired, and, contracting, the elastic fibers of the air vesicles, are strangled. Atelectasis, on the one hand, and accumulation of secretions in the stenosed bronchial tubes on the other, are effective in producing dilatation of the bronchi. In cases in which pleurisy complicated the acute disease, the productive inflammatory process emanating from the pleura sends forth strands of connective tissue into the parenchyma, and these have the same effect as the process just described. Pathologically the lesion is chronic bronchopneumonia, with resulting bronchiectasis. Douglas Symmers,[18] who has made excellent studies of the pathology of cases of influenza that came to necropsy during the last two pandemics in New York, points out that the residuum of bronchopneumonia after organization and overgrowth of connective tissue, should in patients who survive the acute disease result in the formation of bronchiectasis, an expectoration of pus from bronchial fistulas and the like. He is of the opinion that these lesions occur mainly in patients with pleural involvement.

In the vast majority of cases the diagnosis offers no difficulty because the lesion is localized in one of the lower lobes of the lungs. The patient gives a history of an acute disease which was diagnosticated as influenza; he also says that the acute disease was complicated by bronchopneumonia or pleurisy, or both. The fever abated by lysis, but now and then he again suffers from hyperthermia for several days. The cough has not ceased, however, and the expectoration has been profuse some days, while during others it has been scanty or altogether wanting. If the disease has lasted for several months the cough and expectoration may be influenced

[18] Difference in Pathology of Pandemic and Recurrent Forms of So-called Influenza, Jour. Am. Med. Assn., 1920, lxxiv, 646.

by posture. While lying down on one side or sitting up in bed, or on reclining, a fit of coughing is brought on. If large doses of anodyne medication are administered with a view of controlling the cough during the night, the patient has miserable morning hours while the accumulated secretions are being expelled from the chest soon after rising. These patients may be trained to empty the cavities in the chest several times a day, thus acquiring comparative rest and comfort in the intervals.

Hemoptysis is not rare. Usually the amount of blood expectorated is slight, only streaks are noted, but this is sufficient to unduly alarm the patient, and at times his medical adviser. Many cases of more or less copious pulmonary hemorrhage have been seen by the writer among this type of bronchiectatics. The symptoms during the bleeding are not unlike those seen in phthisis, and at times it is very difficult to differentiate these conditions at the first examination of the patient.

While in most cases the course of the fever is undulating, we have met with cases in which the curve was continuous or remittent, as in progressive pulmonary tuberculosis. During the afternoon the fever rises to 100° or 101° F., rarely higher. Others are met with in which the temperature is normal for days or weeks, when suddenly it rises, producing the common constitutional symptoms of fever (Case III). These acute exacerbations are usually concurrent with a lessening of the amount of sputum brought up by the patient, and with the recurrence of drainage of the cavities manifesting itself by copious expectoration of sputum the fever subsides.

During these febrile exacerbations the pains in the chest, usually felt over the affected area, may be intensified. In some cases the pain in the chest is reflected to the abdominal wall or the shoulder of the affected side. This is the case especially when there are adhesions of the diaphragmatic pleuræ.

Dyspnea, subjective or objective, is often a prominent symptom. It is usually due to toxic myocarditis. After the disease has lasted for some time, dyspnea may be caused by pulmonary fibrosis, interference with the lesser circulation, resulting in dilatation of the right heart, and, at times, by cardiac displacement, especially in left-sided lesions in which the pleura has been implicated. The pulse-rate is normal in many instances, but in some tachycardia, cardiac palpitation and precordial distress are prominent symptoms, especially in those in whom toxic myocarditis is pronounced. Acrocyanosis and sweating of the hands have often been observed.

Because they simulate pulmonary tuberculosis, and the traditional notion that influenza is a strong predisposing factor of tuberculosis, these patients are often erroneously diagnosticated and referred to sanatoriums. However, mistakes are easily avoided when the following points are borne in mind: It is exceedingly rare that tuberculosis should follow influenza, as was shown by the

writer elsewhere.[19] The fact that the patient had not coughed before the onset of influenza speaks against tuberculosis even when there are symptoms simulating active phthisis. Physical exploration of the chest usually clinches the diagnosis. The lesion is in most cases found in one of the lower lobes of the lung, usually the left. The resonance is impaired over one base and the breath-sounds are feeble or even absent. Cavernous breath sounds, which are mentioned in many text-books as frequently found in bronchiectasis, have hardly ever been heard by the writer in this class of cases. The most characteristic sign is the presence of coarse, moist rales audible over a circumscribed area of the chest. Cough may provoke these rales in those in whom they are not audible during ordinary or forced breathing. In cases in which the lesion is thus localized in one of the lower lobes the diagnosis is simple. Tuberculosis in which the lesion is confined to a lower lobe, while the apices remain free from pathologic changes, is extremely rare and may be left out of consideration in everyday practice. The fact that, despite its abundance, the sputum is negative as regards tubercle bacilli is confirmatory. In addition, it is noted that with an extensive pulmonary lesion involving one entire lower lobe the patient is not much if at all emaciated. The facies of phthisis is lacking and instead we find cyanosis of the lips and finger-nails. Clubbed fingers are very common.

The following cases have been selected from among many because each illustrates certain points in the diagnosis and course of these pulmonary lesions:

Case III.—M. L., bookkeeper, aged thirty-three years. Had been under the writer's care for minor ailment for several years, and for this reason his lungs and bronchi are known to have been free from any gross pathological changes, until an attack of influenza and complicating bronchopneumonia during October, 1918. The pneumonia was rather severe, but he was on his way to recovery within three weeks after the onset, the temperature dropping by lysis. He continued coughing ever since, and expectorates large quantities of mucopurulent material. He has pain in the lower part of the left side of the chest. His temperature is normal for a week or two, when, without any discernible cause, though he believes that after "catching cold" it rises to 101° F. or even higher, it remains at that level for a few days or a week and then drops again to normal. He can only sleep on the right side with comfort; as soon as he turns on the left side he is liable to provoke a violent fit of cough and expectoration. At times the sputum is streaked with blood. Repeated microscopic examinations of the sputum failed to reveal tubercle bacilli. Various cocci, especially diplococci, are,

[19] Fishberg: Influenza and Tuberculosis, Am. Rev. Tuberc., 1919, iii, 532.

however, found in every smear. Of late he suffers from dyspnea on slight exertion. His lips and fingers are slightly cyanosed, and evidences of clubbing of the fingers have made their appearance. Now and then he suffers from attacks of emetic cough,—after a fit of coughing vomiting is provoked and this gives him relief. His general nutrition has suffered but little. During the febrile periods he loses five or six pounds in weight, but he soon regains it and even more during the afebrile periods. The physical signs show a catarrhal lesion in the lower lobe of the left lung: Impaired resonance, feeble breath-sounds and coarse, moist, consonating rales are audible over that area. There are signs of slight displacement of the heart to the left; the diaphragm is drawn upward.

CASE IV.—M. S., aged thirty-nine years. Past and personal history have no bearings on his present trouble. Seven months before admission to the Montefiore Hospital he sustained an attack of influenza complicated by bronchopneumonia. Ever since the fever subsided by lysis he has kept on coughing, expectorating and has had pains in the chest. Especially annoying to him has been a sense of weakness and aching of the limbs on slight exertion. He states that since he has been out of bed he has had no fever but now and then he has noted some night-sweats. At the clinic of the Department of Health he was pronounced tuberculous in the advanced stages of the disease and referred to this hospital. Physical examination on admission showed a fairly healthy looking man, excepting that his lips and finger tips are slightly cyanosed. The resonance over the chest was found defective above the second rib anteriorly on the left side and over both bases posteriorly. Over the left apex cavernous breath sounds were audible; over both bases feeble breath sounds. Medium sized, moist rales were heard posteriorly on both sides over the bases of the lungs; after coughing some moist rales could be provoked over the left apex.

Throughout his stay at the hospital for six weeks we found his pulse-rate, temperature and respiration normal; blood-pressure 120 systolic and 80 diastolic; urine negative. A slight leukocytosis with an increased proportion of the polynuclear cells was found. A laryngological examination proves negative; only slight deviation of the septum was noted by the rhinologist. Repeated examinations of the sputum, ordinary smear preparations and with antiformin, proves negative as regards tubercle bacilli.

This patient was discharged as non-tuberculous because of the discordance between the findings on physical exploration of the chest and the constitutional symptoms. If the lung lesions disclosed by the physical signs were of tuberculous origin the patient would have suffered from fever, tachycardia, emaciation, etc. Tuberculous patients expectorating as freely as this one did, almost invariably

have demonstrable tubercle bacilli in the sputum. Especially is this true of tuberculous lesions in the lower lobes of the lungs. In this case the physical signs showed clearly a lesion in the upper lobe of the left lung in addition to the basal lesions, and for this reason we kept the patient in the hospital for six weeks, repeatedly examining his sputum and observing his pulse, temperature, etc. As in many others, this case confirmed our observation that tuberculosis hardly ever follows influenza;[20] the few cases observed by the present writer may be considered coincidental. If the patient is reliable, and we are assured that he never had coughed before the onset of influenza, or, what is even better, if we know from personal observation that before the attack of influenza the upper lobes of the lungs were free from pathological changes, we may safely conclude that the localized lesion is the catarrhal or the bronchiectatic form of chronic influenza. At the Montefiore Hospital experience during the past three years has taught us that lung lesions following acute epidemic influenza, irrespective of the symptoms they produce, and the signs elicited while examining the chest, are not tuberculous. This diagnostic principle has helped us materially.

Observation of a large number of cases of this type has disclosed certain characteristics which differentiate these lesions from tuberculous. In many the impaired resonance elicited over the upper lobe is mainly found below the clavicle while in the supraclavicular fossa an almost normal note is brought out; often a tympanitic overtone is audible. In tuberculosis there is almost invariably pulmonary retraction and narrowing of Krönig's areas. The bronchiectatics never have laryngeal and intestinal complications which are frequent among tuberculous with such extensive lesions. With profuse expectoration, fever, night-sweats, emaciation, etc., are the rule in tuberculous lesions, and hardly ever observed in bronchiectatic. A completely unilateral lesion speaks in favor of bronchiectasis.

Radiography is at times of assistance in differentiating these cases. In tuberculosis the shadow indicating airless tissue is found above the second rib, in addition to any other shadows that may be observed, while in post-influenzal bronchiectasis the lung markings are almost normal in that location. The lesion is discerned on the plate exclusively in one of the lower lobes. Signs of a thick pleura and enlarged bronchial glands are commonly observed. The shadow may appear dense one day, while on another, after the secre-

[20] This statement has been questioned by many writers who quote statistics to the effect that a large number of patients admitted to sanatoriums during the past three years state that they have had influenza before the symptoms of tuberculosis became manifest. But it must be borne in mind in this connection that about 25 per cent. of the population in this country has been affected with influenza during the several epidemics waves which occurred since 1918. Especially has the proportion been high among persons between fifteen and forty-five years of age, the period of life when active phthisis is most liable to occur. It is thus to be expected that about 25 per cent. of persons who develop phthisis at present should give a history of having had influenza during the epidemics.

tions have been removed by expectoration, it may clear up, though lung marking are still lacking. Even when the upper lobe is affected, which is rare in bronchiectasis, the cough phenomenon shows that there is little, if any, retraction in bronchiectasis; the parenchyma above the clavicle brightens up during cough, while with tuberculous lesions the reverse is true. In many cases in which fibrosis has been active, or the pleura is implicated in the process, there may be noted some visceral displacement—the diaphragm is elevated and the mediastinum is drawn toward the affected side.

The prognosis in these cases appears to be favorable as regards life, but gloomy as regards relief of the symptoms. The writer has cases under his care acquired many years ago, and thus believes himself to be in a position to state that he has not seen one in which the symptoms have disappeared completely. They keep one coughing, expectorating, are more or less dyspneic and cyanosed though they hardly lose in weight—some even gain in this regard. Their life appears to depend on the undulating course of the disease, with ups and downs. That which they consider "catching cold" consists in acute exacerbations of fever, pains in the chest, profuse expectoration, etc. After a few weeks of misery due to these symptoms they again feel better in a measure for an indefinite time, till they again "catch cold" when the acute symptoms return. During these acute exacerbations, pneumonia is frequently diagnosed because the signs elicited over one of the lower lobes, combined with the fever, pain in the side, etc., are not unlike those of some aberrant cases of pneumonia. Patients met by the writer who have had this sort of bronchiectasis for many years give a history of several attacks of "pneumonia." Some live to an advanced age and finally die from pneumonia, exhaustion due to amyloidosis, dilatation of the heart with edema, etc. In rare cases the end comes through complicating gangrene of the lung.

Pulmonary Suppurations.—The most serious sequels of influenza appear to be pulmonary suppurations of which we meet now more than before the pandemic of 1918–1920. They are serious because of the severity of the symptoms, and the gloomy outlook for recovery.

Pulmonary suppurations occur almost invariably in influenzal patients in whom the complicating bronchopneumonia was of a stormy type. In nearly all cases I have elicited the fact that during the acute disease the physician in attendance gave a fatal prognosis, though ultimately recovery of a sort ensued. Nearly all pathologists who reported necropsies on fatal cases of influenza mention that the number with pulmonary and subpleural abscess was large. Douglas Symmers and Morris Dinnerstein[18] found 35.5 per cent. of fatal cases were associated with the presence of intrapulmonic abscess, which varied in size from minute affairs to purulent foci approximating 2 or 3 cm. in diameter. In one case the upper lobe

of the lung was almost completely replaced by multiple or intercommunicating cavities. The writer has seen several of these cases clinically. While most of the patients with pulmonary suppurations succumb to the acute process, some recover, or at least linger along for several weeks or months.

In nearly all cases of pulmonary abscess of influenzal origin the history shows that the patients had not been relieved from the symptoms of pneumonia, but that for weeks after the onset of the acute disease the symptoms of acute intoxication have persisted. The fever remains high, the prostration is marked, and the patient expectorates large quantities of purulent material, at times fetid, often tinged with blood, and containing elastic tissue. In some cases copious pulmonary hemorrhages have occurred. Pain in the affected side of the chest is a prominent symptom. In the comparatively few cases which are not immediately fatal the fever abates several weeks after its onset and the general condition apparently improves more or less, but sooner or later another acute exacerbation occurs and the patient is again laid up with fever, prostration and pain. Such exacerbations and remissions recur at irregular intervals supplying false hopes of recovery one the one hand, or despair on the other. More or less copious pulmonary hemorrhages occur in many cases and after each bleeding the copious expectoration, the pain in the chest, and the fever may be ameliorated. The general condition of the patient, especially his weight and feeling of well-being oscillate, depending on the pulmonary symptoms and the fever. During the acute exacerbations the patient loses ground, but as soon as he becomes afebrile he picks up again and he may thus hold his own for many months; in the pronouncedly chronic cases he may even be the gainer in this regard, especially when the abscess cavity drains freely. The marked emaciation of advanced tuberculosis, which some cases simulate exquisitely, is never seen with chronic pulmonary abscess, nor is there to be seen the hectic facies of phthisis. However, cyanosis of the lips and finger tips, and dyspnea are dominant symptoms in most cases. Clubbing of the finger may occur within a short time.

Physical exploration of the chest is often deceptive soon after the symptoms of the acute infection have passed. The signs are usually those of a pleural effusion in the lower part of the chest. Exploratory puncture, however, proves negative. Within a few weeks it is noted that while the flatness and feeble breath-sounds remain, there appear coarse, moist, consonating rales audible over the affected area; concurrent with the appearance of these rales the patient also begins to expectorate large quantities of purulent material often mixed with blood. While in some cases the fever declines with the onset of copious expectoration, in most it keeps at high level for several weeks. Then the undulating course mentioned

above begins; at some period the patient may be afebrile to be stricken again with fever after a few days or weeks.

The patient then enters the chronic stage of the disease. The lungs all over clear up, no signs of disease are to be found on physical exploration of the chest, excepting over the site of the lesion where dulness, or flatness, feeble breath-sounds and large, most rales are elicited. In most cases the lesion is in one of the lower lobes; in very few, in one of the upper or the right middle lobe, and several cases in which almost a complete lung was implicated in the suppurative process were seen by the writer. In some cases the odor of the sputum is offensive; it is disagreeable, but it has not the sharp, penetrating, disgusting, or cadaverous odor of pulmonary gangrene. The sputum when collected into a conical glass is seen to separate on standing into three layers, and microscopically elastic fibers are discovered in addition to a variable flora of microörganisms among which Pfeiffer's influenza bacillus is not dominant.

The inflammatory process may reach the pleura and an effusion takes place. But when we have signs of fluid, confirmed by exploratory puncture, we should not forget that there is an underlying suppurative process in the lung and a guarded prognosis should be given. The history will often help in the diagnosis, but the following points may be taken into consideration: In simple pleurisy with effusion the patient coughs, but he brings up little if any sputum, while in cases with abscess considerable quantities are expectorated, at times ill-smelling, or tinged with blood. Rarely copious hemorrhages occur. In several cases under the writer's care the effusion was purulent; in one, sanguineous.

From among many cases observed by the writer during the past two years, the following have been selected as typical:

Case V.—I. R., woman, aged thirty-two years, born in Italy, married. Father died from cirrhosis of the liver, a brother, from meningitis at the age of two. She has been married thirteen years, has had three children and two miscarriages, one induced.

November, 1918, while seven months pregnant, suffered from an attack of influenza complicated by bronchopneumonia, recovered in three weeks. She, however, did not become completely afebrile, and continue coughing, expectorating large quantities of purulent sputum, remained weak, etc. In January 1919 was delivered of a full term infant, followed by a severe postpartum hemorrhage. The cough then became even more aggravated, chills and fever reappeared and she was removed to a hospital where she was told that she had pneumonia in the left lung. Her symptoms at that time were severe cough, profuse expectoration, hemoptysis, fever, sweats and marked dyspnea. For three months these symptoms of "pneumonia" continued and she left the hospital with little, if any, relief. She then entered another hospital where she remained

for ten weeks without seeing any marked improvement. Here she was told that inasmuch as her trouble was of a tuberculous nature, it were best that she seek climatic treatment. Directly from the hospital she went to the Adirondacks where she remained for ten weeks. Finding no relief, she returned to the city, applied to the Department of Health and was referred to the Montefiore Hospital as suffering from pulmonary tuberculosis.

On admission, October 9, 1919, we found her suffering from severe incessant cough, profuse expectoration of purulent material, at times fetid, or tinged with blood. Physical examination showed that the

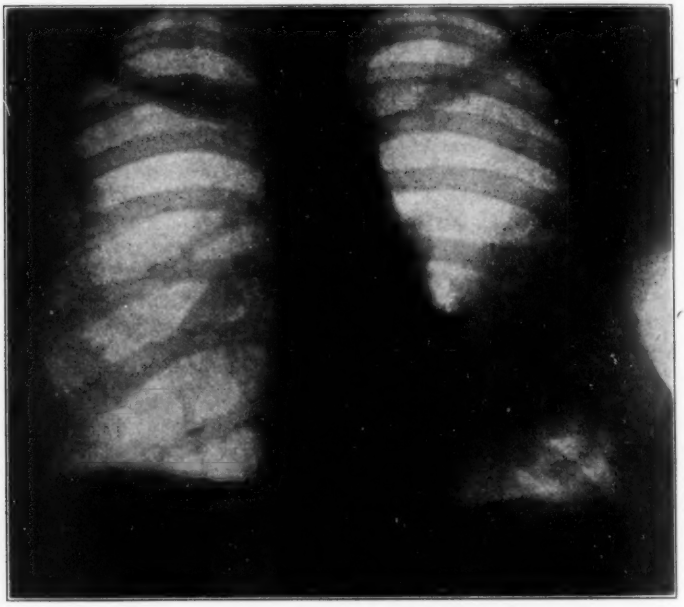

FIG. 1.—Pulmonary abscess in lower lobe of left lung.

lower lobe of the left lung did not breathe: flatness, absence of vocal fremitus, feeble breath-sounds, and large, moist, consonating rales. The resonance elicited over the right upper lobe was impaired and the breath-sounds bronchial in character. We thus found one pulmonary lesion in the right apex and another more serious and extensive one, in the lower lobe of the left lung. There were also audible moist rales all over the chest, especially over the upper lobe of the left lung. Her temperature ranged between 100° afternoons and 98° F. mornings; the pulse-rate 85 to 95 per minute. The discordance between the extent and activity of the pulmonary lesion and constitutional symptoms was at once noted: She appeared

well nourished, her best weight having been 145 pounds and on admission it was 132, showing that despite the extent and activity of the disease lasting eleven months, there had not occurred that cachexia characteristic of phthisis of this activity, extent and duration. All this pointed to a non-tuberculous pulmonary process.

The radiographic plate (Fig. 1) showed a large, somewhat oval shaped, well defined shadow occupying the middle third of the left lung field. Evidences of pleuropericardial and diaphragmatic adhesions were also noted. In the right lung signs of hilus fibrosis associated with bronchial dilatation were found and also a number of fibrous bands running across the middle of the lung field. The fact that the radiographic picture of the right upper lobe was not that characteristic of tuberculosis, and that the heart was normal in size and appearance, confirmed the clinical opinion that the lesion was non-tuberculous.

The examination of the sputum, made eight times, failed to disclose any tubercle bacilli; various cocci, mainly staphylococci albus were found. The urine was negative, the blood-pressure 145 systolic and 100 diastolic, rather high for tuberculosis. A blood count also pointed against tuberculosis: 15,000 whites, and 75 per cent. polynuclears. Inasmuch as the radiographer insisted that there was fluid in the left pleura, though the physical signs—the presence of large, moist rales—were against this view, several exploratory punctures were made, one with a large caliber lumbar puncture needle, but all failed to bring out any fluid. On entering the patient's lung with a needle, about ½ c.c. of thick, yellowish, foul-smelling pus, not unlike the matters she expectorated, was obtained.

An attempt was made by the writer to induce an artificial pneumothorax with a view of collapsing the left lung and thus assist in draining the abscess cavity, but owing to pleural adhesions no gas could be injected into the pleura.

On October 20 the patient was transferred to the non-tuberculous division of the hospital. The treatment was mainly postural. It was found that she sleeps on her right side, and that turning on her left side she coughs and expectorates profusely. Raising the foot of the bed and placing her on her right side for fifteen to twenty minutes several times a day, so that gravity helps in clearing the pulmonary cavity, has had a marked effect on her condition. She gained in weight, reaching 150 pounds, more than she ever weighed, and looks and feels well. Her temperature has been normal, for weeks, though now and then, when drainage is retarded, or when she neglects to recline on her right side for a day or two, the temperature rises one or two degrees, to decline again after postural treatment is applied. She was discharged March 18, 1920, greatly improved. She still coughs and expectorates, but her general condition is excellent.

CASE VI.—I. T., woman, aged twenty-seven years, admitted May 29, 1919. Her past history is of no importance, excepting perhaps that she had typhoid fever at the age of ten. Taken sick with influenza January, 1919, the initial symptoms were chills, fever, backache, cough, hemoptysis and pain in the right side of the chest. In a communication from the hospital, in which she was cared for at that time it is stated that she suffered from influenza complicated by bronchopneumonia. Because of the lingering lung lesion after five weeks' treatment, she was told that inasmuch as her trouble is of a tuberculous nature it is best for her to go to a mountainous climate. She went and remained there for six weeks, but the cough

FIG. 2.—Abscess in lower lobe of right lung.

and profuse expectoration persisted, chills and fever, pains in the chest and weakness kept on annoying her. She returned to the city and was readmitted to the hospital where she was again told that her trouble was tuberculous, and she was referred to the Health Department. She was then admitted to the Sea View Sanatorium where she remained a short time and then transferred to the Montefiore Hospital under the writer's care.

On admission we found her apparently well nourished, though running high fever, of the continuous type, had frequent chills, sweats, pain in the chest, coughed and expectorated profusely. Repeated pulmonary hemorrhages occurred, some of which were quite copious. The sputum was malodorous. Physical exploration

of the chest showed that the main lesion was in the lower lobe of the right lung, over which the resonance was flat, the breath-sounds feeble, and large, moist rales and a friction sound were audible. The vocal fremitus was abolished over that area. However, the upper lobe of the right lung showed also pathological changes—impaired resonance and distinct bronchial breath-sounds. No changes at all could be discovered in the left lung. Repeated examinations of the sputum failed to show the presence of tubercle bacilli, but Gram-positive diplococci were found in abundance. The blood count showed 4,000,000 reds, 34,000 whites, and 75 per cent. lymphocytes; hemoglobin 70 per cent.

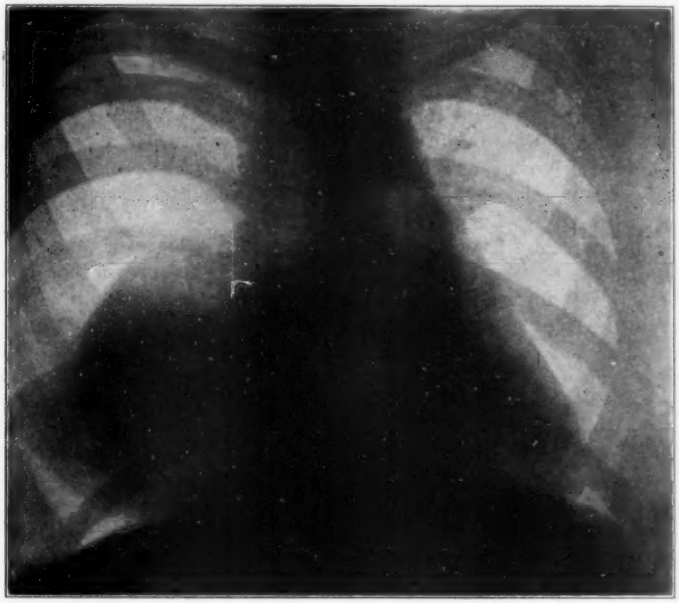

FIG. 3.—Same case as in Fig. 2. Complete collapse of right lung by artificial pneumothorax. The abscess cavity is seen surrounded by a thick capsule.

The radiographic plate (Fig. 2) also pointed against tuberculosis. The two apical fields were apparently free from distinct changes; a somewhat oval-shaped shadow obscured the middle portion of the right basal field. The rest of the lungs were clear.

The clinical, bacteriological, radiographic and hematological data showed clearly that we were dealing with a lung abscess of influenzal origin. The usual treatment applied failed to be effective in relieving her symptoms, the incessant cough, profuse expectoration, the fever, the chills, etc., persisted. The following, culled from the bedside notes, give some idea as to the course of her ailment:

July 6, 1919. Severe pulmonary hemorrhage, lost about eight ounces of blood.

July 30. A more copious hemorrhage.

August 12. Patient has been bleeding profusely for three days. Horse serum administered with no visible effect.

August 17. Hemorrhage profuse and threatening. Induced an artificial pneumothorax, injecting 600 c.c. of air. Hemorrhage stopped promptly. On the three succeeding days further inflations of gas into the pleura were given, obtaining complete collapse of the right lung. The pulmonary hemorrhage was thus controlled for ten weeks. But no relief in the general symptoms was apparent. The fever, chills, cough, expectoration, etc., continued unabated. Considering the thick capsule around the abscess (Fig. 3) it is clear that the air in the pleura was not effective in obliterating the abscess cavity by compression. However, we continued the pneumothorax treatment and on October 15, signs of a pleural effusion, a hydropneumothorax,—succussion sound, metallic tinkle, flatness over the lower thirds of the right chest, etc.—made their appearance. Concurrently the pneumothorax was no more effective in preventing pulmonary hemorrhage; she began again to bleed profusely. Puncture showed that the effusion was purulent.

October 22. The septic fever, dyspnea, cyanosis, weakness, etc., not being relieved by the usual therapeutic measures, a thoracotomy was performed, and several quarts of foul smelling pus removed from the right pleura. Patient died four hours after the operation.

Resume.—In many patients attacked by acute epidemic influenza certain sequels are left in the respiratory tract after the acute disease had run its course. A large number remain with subacute rhinopharyngitis; some with general bronchitis, and now and then we meet with patients in whom the residual lesion is a localized bronchitis. When the latter affects an upper lobe of a lung, it is very difficult to differentiate it from pulmonary tuberculosis. When these sequels are instrumental in keeping the patient weak and debilitated for weeks or months, which is often the case, this, in addition to the cough and expectoration, may lead to a diagnosis of pulmonary tuberculosis. More serious pulmonary lesions are bronchiectasis and lung abscess which have increased in frequency since the last pandemic of influenza. Bronchiectasis remains in cases in which influenza was complicated by pneumonia or pleurisy, or both. The diagnosis is at times very difficult mainly because of the ancient notion that influenza is a strong predisposing factor to tuberculosis. When the lesion is found strictly localized in one of the lower lobes of the lungs, and this is the case in the majority, tuberculosis should be excluded for this reason alone. In those in whom the lesion is in an upper lobe, only repeated sputum examination decides, though the fact that the disease began with influenza,

that emaciation is not pronounced, that fever is lacking, the pulse-rate is normal, and that there is obtained clear resonance above the clavicle, etc., should be counted against tuberculosis. The more severe lesions in which pulmonary abscess remains after influenza the diagnosis may be made along the same lines as in bronchiectasis, and in addition note should be made of the fact that the sputum is abundant, at times fetid, the fever continuous or undulating, the pain in the chest and the physical signs, all of which combine to clear up the diagnosis. If several examinations of the sputum fail to disclose tubercle bacilli the diagnosis may be safely made. Leukocytosis, with an increased proportion of polynuclear cells have the same significance.

STUDY OF A CASE OF UNEXPLAINED LOW CARBON DIOXIDE COMBINING POWER OF THE BLOOD.

By Leon Jonas, M.D.,*

AND

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PHILADELPHIA.

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The following case is reported because of the persistent occurrence of a low carbon dioxide combining power of the blood and an increase in the rate and depth of respiration in an individual in whom no adequate explanation for these phenomena could be discovered. The patient's chief complaint was shortness of breath and a feeling that his heart beat fast; the abnormal respiration was sufficiently marked to attract immediate attention when one approached the patient. It was this observation which led to the further special study of the case as well as the fact that the physical examination revealed no cause for the obvious increase in respiratory frequency; nor did the routine laboratory studies reveal any of the disease conditions which we are accustomed to expect as leading to dyspnea. No justification for a diagnosis of cardiac, pulmonary or renal disease was found, nor was there any evidence of diabetic acidosis; in fact, no evidence of disturbed acid-base equilibrium other than the constantly low plasma carbon dioxide combining power. There was no fever.

In brief, the patient presented an unusual picture which we are unable to explain, and we are reporting the facts without attempting

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to draw any conclusions. Undoubtedly a reasonable explanation exists, to become apparent only after further facts are known.

CASE REPORT.—G. H., male, aged sixteen years, entered the University Hospital on February 9, 1920, complaining of shortness of breath and a feeling that his heart beat fast. The history in brief was as follows: He was in perfect health until about five weeks before admission, when he had run for over an hour without any previous training. He was accompanying a boxer who was training, and they ran "at least five miles." There was no special discomfort at the time, but three days later he became conscious of the beating of his heart. A week later he had an acute attack of dizziness and vomiting, which continued for two days. He stated that he had not been well since the overexertion in running, and he claimed to have lost ten pounds during the two weeks prior to admission. Previous medical history was negative and there was nothing of importance in the social or family history.

The patient was a healthy looking individual, obviously a mouth-breather. It was noted at once that the breathing was more rapid and deeper than normal; the rate varied between 24 and 32 to the minute. The hands and fingers were somewhat cyanosed, but not markedly so; the blood-pressure was low: systolic 96, diastolic 68. Definite tonsillar enlargement was present and also a slight general adenopathy. In all other respects the physical examination was negative. Repeated examinations of the heart by several examiners and by fluoroscopy and electrocardiography revealed no alteration from the normal. The lungs were normal by physical examination; roentgenograms revealed no pulmonary pathology nor any mediastinal abnormality. Neurological examination was negative.

The routine laboratory examinations were as follows: Blood count: Erythrocytes, 4,410,000; leukocytes, 7000: hemoglobin, 71 per cent. Differential count: Polymorphonuclear neutrophiles, 73 per cent.; lymphocytes, 22 per cent.; large mononuclears, 4 per cent.; transitionals, 1 per cent. The serologic test for syphilis was negative. As is our custom, specimens of urine were sent to the laboratory on the first, third and fifth mornings after admission. These showed striking variations in the concentration, albumin content and microscopic findings. Such changes are familiar to all hospital physicians and result at least in part from the increase in fluid intake incident to hospital care.

	Color.	Sp. gr.	Albumin.	Microscopic.
1.	Dark amber	1029	Heavy cloud	Light and dark granular casts.
2.	Amber	1015	Very faint trace	0
3.	Straw	1007	0	0

In all other respects the examinations were negative. On the day of the third specimen the phthalein elimination was 60 per cent.

in two hours and the blood-urea nitrogen was 15 mg. per 100 c.c. of blood.

Other special examinations which should be mentioned included a negative examination of the eye-grounds and negative roentgenograms of the pituitary region. Roentgenograms of the teeth revealed an abscess at the root of a molar tooth.

The following table will detail the further study of the case:

1920.	Sod. bicarbon., gm.	Blood plasma, CO_2 vol., per cent.	Urea N., mg. per 100 c.c.	Urine.				
				Amount, in c.c.	Specific gravity.	Reaction.	NH_3N.	Titratable acidity, N/10 NaOH
Feb. 14	5	29.0	15					
15	20							
16	5	42.5						
17	..	..	..	2840	..	Acid	0.30	249.2
18	..	..	..	2540	..	Acid	0.24	223.1
19	..	48.2	..	3000	..	Acid	0.44	368.0
20	..	53.0	15	2800	..	Acid	0.59	396.0
21	..	52.0	..	4000	..	Acid	0.59	747.0
22	..	..	..	5000	1.004	Acid	0.26	571.0
23	..	47.0	..	4760	1.005	Acid	0.36	786.0
24	..	42.0	..	3850	1.008	Acid	0.36	857.0
25	..	47.0	..	3620	1.008	Acid	0.36	
26	..	46.0	..	3400	1.004	Acid	0.33	439.0
27	20	46.0	..	..	..	..	Spec. lost	
28	20	48.0	..	3870	1.007	Acid	0.22	104.5
29	20	..	..	3160	1.008	Acid	0.20	104.5
Mar. 1	20	50.0	..	2310	0.008	Acid	0.25	
2	25	54.0	..	3920	1.008	Acid	0.18	170.5
3	20	59.0	12	2660	1.010	Sl. alk.	0.12	Neutral
4	25	55.0	..	2230	1.011	Sl. alk.	0.18	120.0
5	..	..	..	1910	1.008	Acid	0.27	176.0
6	..	49.0	..	..	..	..	Spec. lost	
7	..	..	..	2320	1.009	Acid	0.42	288.0
8	..	..	..	2680	1.010	Acid	0.46	171.0
9	..	54.0	..	1780	1.010	Acid	0.21	363.0
10	..	..	..	940	1.016	Acid	0.31	284.0
11	..	55.0						
12	..	55.0	12					
15	..	52.0						
17	..	43.0						
18	..	48.2	12					
22	..	47.9						
23	..	47.0						
27	..	49.0						
30	..	..	12					
April 1	..	53.0						
6	..	52.0						
14	..	53.0	12					
June 1	..	55.0	17					

Interest was aroused by the report that the plasma carbon dioxide combining power was reduced to 29 volumes per cent. and a corresponding low alveolar carbon dioxide tension. No observations

were made to determine the influence of the low CO_2 combining power of the plasma on the power of the hemoglobin to combine with oxygen.

The examination of the data contained in the protocol together with an absence of both a ketonuria and a glycosuria and the presence of a normal blood sugar immediately excluded diabetes as the cause of the low CO_2 combining power of the plasma.

The examination of the urine for lactic acid was negative for any abnormal production of this acid.

We feel that nephritis, as has been previously stated, can be eliminated by the constant absence of urea retention and the normal phenolsulphonephthalein elimination. Albumin and casts were found in the first examination of the urine, but all subsequent examinations were negative. Although a marked polyuria and a corresponding low specific gravity were present for a number of days the kidneys were able to concentrate, as was shown by the first urinary examination when the specific gravity was 1029, and on April 27, 1920, when the intake of fluids was greatly restricted, with a result that the output was reduced to less than 500 c.c. per twenty-four hours and the specific gravity raised to 1029. We do not feel that the polyuria is especially peculiar to the condition because of the great ingestion of fluids, particularly water and milk. The striking feature of the case is the low CO_2 combining power of the plasma with the constant normal output of ammonia nitrogen and a normal titratable acidity, except from February 20 to February 24, when the titratable acidity was above normal. The cause of the increased titratable acidity at that time is unexplained. Although a total of 30 gm. of bicarbonate of soda was given between February 14 and the morning of February 16, we feel that it did not influence the ammonia nitrogen and titratable acidity on the subsequent days, particularly in view of the continued low CO_2 combining power of the plasma.

Henderson[1] has shown that hyperpnea may cause a marked lowering of the carbon dioxide combining power of the plasma with a normal urinary ammonia and titratable acidity. We investigated the possible application of this idea to our patient, assuming that the rapid, deep breathing was due either to an oversensitive respiratory center or stimulation of the center by a neoplasm, perhaps of the pituitary, in view of the polyuria. Negative roentgenographic findings excluded a pituitary tumor as the cause. If due to overventilation then the depression of the respiratory rate should raise the blood CO_2 combining power with no ill-effects, such as would result if due to the usual clinical causes of acidosis. To test this possibility, morphin sulphate was given hypodermically from

[1] Jour. Biol. Chem., 1918, xxxiii, 345, 355, 365.

February 18 to February 21. By February 21 the respiratory rate was reduced to 16 per minute, and during this period the blood CO_2 reached its highest figure, except early in March, when the high figure was due to the administration of sodium bicarbonate. Unfortunately the specimen of blood which was taken just before the beginning of the administration of morphin sulphate was lost, due to an accident. After the affects of the morphin sulphate had ceased the blood CO_2 again fell. No ill-effects on the patient were observed during this experiment.

Although these experiments seem to admit the possibility of overventilation as the cause of this unusual phenomenon in the patient, we do not feel that the data at hand is sufficiently conclusive to permit this or any positive diagnosis. The sensitiveness of the respiratory center was tested on March 3, after the blood CO_2 had been raised to normal, by the administration of sodium bicarbonate from February 27 to the date of the experiment. The method employed was to have the patient breathe normal air and then air containing 5.2 per cent. of CO_2, recording the rate and depth of the respirations on a kymograph. It was found that the breathing of air containing 5.2 per cent. of CO_2 caused a turn-over of air twice that observed before the CO_2 was increased. This is considered a normal reaction for that concentration of CO_2.

Other possible explanations have to be considered, but none appear satisfactory. Hysteric tachypnea, such as was described by S. Weir Mitchell, and such as is not infrequently observed clinically, is apparently ruled out by the persistence in this case of the respiratory rapidity during sleep. The acute attack of indigestion with vomiting can scarcely be considered prolonged enough to have disturbed the patient's acid-base equilibrium for so long a period, nor were the alterations in this case those seen after vomiting, starvation or in "cyclic vomiting," such as ketonuria, etc.

EMPYEMA THORACIS: AN ANALYSIS OF FIFTY-SIX CASES IN THE INDIANA UNIVERSITY HOSPITAL.*

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Empyema literature of the last two years is voluminous enough to give the average reader mental anorexia. The subject has necessarily been clouded with uncertainty, so rapid have been the changes in conception of both pathology and treatment. The aim of this

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analysis of 56 cases is not only to tabulate the results, but, further, to ascertain by comparison with other series the soundness of our position on the question.

Mortality. Our cases have been civilian and of both sexes, varying in age from sixty-four years to four months. The average, 22.8 years, is not far from 21.6 years, Ransohoff's[1] civilian average at the Cincinnati General Hospital. Few of our cases have had the soldier's rugged constitution to help combat infection, which in a measure justifies our 7.1 per cent. mortality in the face of the 4.3 per cent. death-rate of the Empyema Commission.[3] Then, too, one of the deaths was more, strictly speaking, a traumatic pyothorax, the patient (a man of sixty-four) dying eight weeks following a gunshot wound of the lung. Another one of our fatal cases entered the hospital moribund and died a few hours after admission, physical examination having revealed, aside from the empyema, an active Neisserian infection, a fulminant nephritis and associated general edema. The third death was in a child of three and a half years, whose empyema followed a virulent measles pneumonia. In the fourth death, pleural pus pockets were complicated by a large lung abscess. That our death-rate does not approach the 28 per cent. of Vaughan,[4] the 12 per cent. of Eggers[5] and the 15.6 per cent. of Willard Stone's second series[6] is probably referable to the fact that the cases represent no single epidemic, and hence perhaps not such virulent infection. On the other hand many have been eleventh-hour emergencies: the cases of empyema gravitating to a state charity hospital we have found often to be cases that the home doctor has "given up for dead."

Clinical Data. Past history of nose, throat and chest troubles has been infrequent among our cases. (Percentages are noted in Chart I.) These low figures only reëmphasize the long recognized fact that past history and pulmonary predisposition are hardly important factors in the etiology.

Eggers was able to develop a history of antecedent pneumonia in almost all of his cases. While 44 per cent. of our cases followed frank pneumonia and 22 per cent. influenzal pneumonia, gunshot wounds, pertussis and measles pneumonia have also been precursors of the condition. (See Chart II.) In 8 per cent. there were other suppurative body foci, *e. g.*, pus appendix, cellulitis of the leg, gluteal abscess, etc. (In 20 per cent. of the cases there was a family history of tuberculosis.)

Diagnostic Features. *Temperature.* Though Vaughan has noted cases that were completely afebrile, picked up only on routine examination, all of ours have shown a perceptible amplitude (minimum 1 degree, maximum 7 degrees, average 3.85 degrees).

Pulse-rate. The importance of a high pulse-rate—already emphasized by Stone—we have had occasion to observe in this series. The general average of pulse-rates was 104—none of the cases showing a rate below 80.

Leukocyte Count. Our maximum white blood count was 28,000, minimum 8000, average 17,000.

X-ray. In a certain number of cases the fluoroscope has been of great value, but in others quite deceptive. Our observations certainly agree with those of Vaughan, that it is in interlobar empyema that fluoroscopy is of the greatest value.

Urine. Less than half of the cases have voided normal urine (32 per cent.). The findings are conveniently tabulated:

Albumin	14 per cent.
Albumin and casts	30 "
Albumin and pus	18 "
Albumin, casts and pus	4 "

Physical Signs. The four physical signs of greatest diagnostic value in the series have been (1) lagging or retraction of the affected side (in 88 per cent. of cases); (2) dulness (84 per cent.), (3) distant or absent breath sounds (80 per cent.), (4) diminished tactile or vocal fremitus (74 per cent.). Grocco's triangle and cardiac displacement have been surprisingly rare physical signs.

The chronicity of many of the cases has resulted in the frequency of other symptoms less common in military practice; 26 per cent. of our cases showed very extreme emaciation. Only two of these had other cause for the symptom than the present trouble, and these two were tuberculous. There was definite hypertrophic pulmonary osteo-arthropathy in 26 per cent. of the series. In half of this number the process was over a year old when we received the cases. Sinus scars were present in 22 per cent. of the series.

Treatment. (*a*) *Underlying Principles.* Graham and Bell[7] have ingeniously shown, in both dog and man, (1) that the normal thorax is in reality a single cavity, the mediastinum acting much as a rubber membrane in dividing it into two compartments, each one of which is necessarily sensitive to changes in pressure in the other; and (2), that the normal pleural cavity will tolerate an opening of a certain determinable size (about 2 by 5 cm.). In pneumonia or other conditions producing diminution in available breathing space there is also diminution in the size of the thoracotomy wound that can be tolerated. In view of these factors it is argued that with too large an opening an alarming situation can develop—pneumothorax, with pulmonary collapse on the open side and bulging of the mediastinum to the opposite side with subsequent excursion limitation and consequent embarrassment of the sound lung (Eggers). This is claimed to be the train of events after opening the general pleural cavity. Whether or not this sequence of conditions actually occurs is after all of academic rather than practical interest, since opening of the general pleural cavity is a procedure never indicated in the treatment of empyema.

Quite different are the factors to be reckoned with in the opening

of an empyema cavity. The pathologic processes generating an empyema include the walling off of a pleural compartment in which the pus is enclosed.* Opening this does not mean opening the general pleural cavity, which is excluded by a definite barrier of adhesions. It is generally acknowledged by the best authority[3 5 6] that until this barrier is well organized, aspiration is the only scientifically sound and thoroughly safe method of removing fluid. Vaughan even advises no other surgical interference than repeated aspiration as the case progresses, provided the patient is clinically gaining ground; and Stone reports 11 per cent. of 310 cases cured with no further drainage. In one of our cases, a boy of four years, with bilateral empyema, aspiration alone has taken care of one side.

Though the intercostal trocar and catheter (with negative pressure) are theoretically permissible and in some cases have been successfully used at this stage of adhesion formation, there is always the danger of a flaw in apparatus, a break in technic, with the resultant serious accident, pneumothorax. The danger is, of course, only exaggerated if the other lung is pneumonic.[9] When once the cavity is walled off the problem becomes one of simple drainage, and as Hartwell[10] emphasizes, collapse of the lung will not follow open operation, for the very obvious mechanical reasons already stated.

(*b*) *Operative procedures.* These may be grouped and considered thus:

I. Acute Empyema.† A. *Aspiration.* Aspiration, the treatment *par excellence* during the formative stage, is occasionally sufficient in well-encapsulated accumulations. It was the only measure in $3\frac{1}{2}$ per cent. of our cases. In one the puncture was the last resort on a patient who entered the hospital moribund and died the same day. Another, delivered ten days before, made an uneventful recovery after several taps. Reference has already been made to the third case, a boy of four, with bilateral empyema.

B. *Open Intercostal Drainage.* In 2 cases of rather abortive type intercostal drainage was deemed sufficient. One was irrigated for several days with normal salt solution. Both left the hospital three weeks after operation.

C. "*Closed Methods.*" Moschcowitz,[11] introducing an intercostal tube of good size (preferably in the eighth interspace, posterior axillary line) secured by suction probably the best drainage of any of the closed intercostal methods. Diederich's[12] method in principle is very similar. Mozingo[13] introduces the added feature of glycerin-formalin injection. In considering these methods the pathologic conditions should be kept clearly enough in mind to avoid the mistaken conviction, only too often expressed, that negative pressure

* Vaughan[4] has shown that this encapsulated empyema is the dominant type.

† Since differentiation depends on so many features, the terms *acute* and *chronic* in referring to empyema are certainly unhappy. We use them arbitrarily as follows: *acute* applying to cases never before drained; *chronic*, those with sinuses.

is preventing pulmonary collapse. The value of negative pressure at this stage is only in mechanically aiding in drainage. Adhesions have by this time precluded the possibility of collapse. It should also be remembered there is no excuse for this type of drainage before the empyema is excluded from the general pleural cavity.

Müller's[14] very excellent commentary on these "closed methods" is worthy of repetition in full: "It seems to me that there is but little difference in the methods of Mozingo, Diederich or of Moschcowitz. They will cure a certain percentage of the cases, but are liable to pocketing, persistent cavity or relighting of latent infection. They will be most successful in the streptococcic group. The method of Moschcowitz is the best, because he uses the largest tube and therefore gets the best drainage, that of Mozingo the worst, because he gets no drainage at all but depends on chemical sterilization for the results."

Another very significant paragraph of Müller's review reminds that closed methods fifteen years ago had a vogue and then went into the discard (Shiller[15]). This item in the history of empyema is certainly suggestive and should stir in the profession a wholesome skepticism until the next five years show closed method cases to be non-recurrent.

D. *Rib Resection.* Since copious drainage the first twenty-four hours is of the utmost importance, and anything less than thorough drainage is inexcusable, rib resection has seemed to us the only safe method of treating well walled-off cases. This opinion, shared by many others,[3 5 6 10 16 17 26] has the sanction of years and has already outlived one "closed method" era a decade or more ago.

Sixty per cent. of the cases in this hospital have been so treated, the seventh and eighth ribs being the commonest sites of operation. Two resections were in the anterior, six in the posterior, and twenty-two in the mid-axillary line. The observation of Keyes,[16] that posterior axillary line wounds offer the best drainage seems to be substantiated by these results, for the average postoperative stay of the midaxillary cases was five weeks, anterior axillary four and a half weeks, posterior axillary four weeks. These figures compare favorably enough with the postoperative forty days of Diederich's closed method and the five or six weeks of Rodman.[18]

Among the objections raised to rib resection have been pain, serious and often fatal intercostal vessel hemorrhage, lung collapse, etc. Lung collapse we have never observed in a single case of this series. We cannot conceive of such an accident occurring if ordinary care is taken to await encapsulation, the existence of which aspiration, clinical history and physical signs will clearly evidence. The danger from hemorrhage we believe overestimated. In what cases of this series the intercostal vessels have been injured, bleeding has stopped spontaneously, without ligation, and soon enough to occasion negligible operative delay. In our experience thorough infiltra-

tion of the skin and blocking of the intercostal nerves with novocain renders rib resection a painless operation. One recent case, a physician, assures us that his side was completely anesthetic during the entire procedure. (Of course, a rib snapping in the rongeurs is hardly a reassuring sound and will ever be disconcerting to the neurasthenic!)

E. *Subsidiary Therapeutic Measures.* 1. Irrigation: Dodge and Eggers are skeptical about irrigation, and Babcock,[19] on departure from Fort McPherson, left 80 empyemas still draining which had been so doing for a year despite Dakin irrigations. However, the results of Stevens[20] would seem to indicate that the judicious use of Dakin's solution is of value. Of his 123 cases, 56 treated by simple drainage showed 25 per cent. recurrence; 67 treated by drainage followed by Dakin irrigations showed only 12 per cent. recurrence. Müller's caution is timely, that Dakin's solution must be evaluated as only a surface disinfectant, not capable of sterilizing the depths of infected pleura. Irrigation (with normal salt solution) has been used in but one of our cases.

2. Glycerin-formalin Instillation: Glycerin and formalin, originally used years ago by Murphy, has been instilled according to varying technics by Sherrill,[25] Diederich, Mozingo, and Rinehart. Diederich believes the practice of little advantage over simple aspiration. We have had no experience with this method.

3. Medical Treatment: Medical treatment in this series has consisted of little more than morphin p. r. n. immediately after operation and a 3000 to 4000 calory diet. Eggers mentions the importance of the patient's position in favoring drainage. In our experience the first notch of the Gatch bed offers a valuable alternative to the supine posture.

II. Chronic Empyema. Under this head we include cases (*a*) with persistent draining sinuses following previous operations and (*b*) with scars and reaccumulations of pus. Treatment in these cases has been directed solely toward one end—the obliteration of the cavity. In some instances it has been sufficient merely to resect ribs and allow parietal pleura to collapse into the depths of the cavity; in others decortication has been necessary because of pleural rigidity. The series consists of 11 cases; 4 of these had been operated on prior to admission to this hospital and had an average past duration of two years. In these, operation consisted in removing subperiosteally (under general anesthetic) portions of from three to five ribs over the cavities. The average post-operative hospital stay was six and a half weeks.

In the seven remaining cases rib resection was done as a deliberate preliminary step toward thoracoplasty, the cavities at initial operation presenting anatomic features which made the necessity of further operation quite obvious. The average period between operations was five weeks. All the secondary operations but one

were done under general anesthetic (ether). (Wattenberg[21] also prefers general anesthesia for secondary operative work but uses nitrous oxide.) None of the eleven cases was in the hospital longer than eight weeks after operation—and the average stay was four and a half weeks. There was one death—a thoracoplasty mortality of 9 per cent.

Years ago Schede[22] claimed that when pleurisy becomes purulent a thick fibrin membrane covers the pleura, but that this can be stripped off months or even years later, leaving a relatively normal pleural surface. Often as early as the tenth day (Lilienthal[23]) this inflammatory covering of the visceral pleura, having become tough, can very materially interfere with the lung expansion. During the earlier stages of the process this immobilization is protective. Later the indication for lung splinting disappears. At this stage Lilienthal, under a general anesthetic, separates the ribs, incises the pleural cavity and mobilizes the lung by freely incising the expansion-limiting membrane around the visceral pleura. The Lilienthal operation in the hands of Whittemore[2] has given slightly lower mortality than ours—$8\frac{1}{4}$ per cent. of 12 cases. But Lilienthal himself[24] has reported 3 deaths in one series of 20 cases.

The Tinker-Wattenberg procedure would seem to offer a less dangerous alternative to thoracoplasty, but we have not yet had occasion to try the method.

Summary. *Clinical Data.* In a series of 56 cases of empyema thoracis at the Indiana University Hospital the mortality has been 7.1 per cent. Most cases followed pneumonia, though injury, pertussis, measles, etc., have also been antecedent conditions. Twenty per cent. had familial tuberculosis, but a negligible percentage gave personal history of pulmonary predisposition.

Signs and Symptoms. The cases showed an average febrile amplitude of 3.8 degrees, average pulse-rate of 104 (none below 80) and an average leukocyte count of 17,000. Less than one-third voided normal urine—and 30 per cent. showed definite evidence of renal involvement.

Lagging or retraction of the affected side, dulness, distant or absent breath sounds, and fremitus absence were the outstanding physical signs (in the order of their frequency of occurrence).

Treatment. In view of the fact that "closed methods" (and we do not include aspiration here!) would seem based on a faulty conception of the pathologic physiology of the chest in empyema, the treatment of acute cases in this series has been palliative aspiration until cicatrical exclusion of the general pleural cavity has made rib resection the operation of safety and choice. Sixty per cent. of these cases have had rib resections—usually the seventh or eighth in the midaxillary or posterior axillary lines. The average postoperative hospital residence has been four and a half weeks, the

posterior axillary line cases leaving the hospital first. We profess no experience in glycerine-formalin instillation.

In chronic empyema the aim has been cavity obliteration by subperiosteal rib resection and at times parietal pleura extirpation. Our mortality with this plan of treatment is 9 per cent. in 11 cases, slightly above the 8¼ per cent. (in 12 cases) of Whittemore, who performs the Lilienthal operation. However, Lilienthal with his own method has reported 3 deaths in 20 cases.

The writer wishes to acknowledge many helpful suggestions, during the preparation of the work, from Dr. W. D. Gatch, Professor of Surgery.

CHART I.—PREDISPOSING PAST HISTORY.

Total number of cases	100 per cent.
Cases with frequent chest colds	8 "
Cases with frequent head colds	6 "
Cases with repeated sore-throat	6 "

CHART II.—ANTECEDENT TROUBLE.

Total number of cases	100 per cent.
Frank pneumonia	44 "
Influenzal pneumonia	22 "
No definite clinical entity	22 "
Gunshot wound of chest	4 "
Whooping-cough	4 "
Measles pneumonia	4 "

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A RECORD OF EXPERIENCE WITH CERTAIN PHYSICAL EFFICIENCY AND LOW OXYGEN TESTS.

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The student of aviation medicine has been confronted with the problems of protecting the flier against the effects of physical deterioration and the effects of altitude, low barometric pressure and deficiency of oxygen.

The call for a measure of health and physical fitness comes from the fact that the aviator has need of all his physical energy and intelligence. Flying requires an active, well-balanced, decisive mind and sound, quick, reflex actions. The aviator must be able to recognize at once the slightest difficulty with his machine. His senses must give him accurate information of changes in the rhythm of his motor, of the sing of air across the wires of the machine and of his position in space. He must be master of his impressions and ready to make prompt decisions in a calm, cool manner. It is now clearly recognized that the aviator's reactions to stimuli are slowed down or disturbed by disease, worry, fatigue, excessive use of alcohol and other excesses. Such influences may cause a delay of a second, or part of a second, in correcting an error in difficulties in the air or in landing which may mean the difference between a crash and safety. The medical adviser requires tests that will reveal the degree of loss in efficiency in order that he may intelligently say when the aviator should not fly.

The ability to endure altitudes well and without loss in efficiency is dependent upon the ease and quickness with which certain adaptive adjustments are made. There are marked individual differences in this respect. Some men adjust so well that they are not disturbed by heights which render the average person quite inefficient. A few men fail entirely to respond to altitude and become inefficient at relatively low altitudes. The flight surgeon finds it advantageous to have the fliers under his supervision, classified as to their ability to compensate to the effects of altitude.

In this paper we shall report the results of a study of 128 aviators who were subjected to the Official Altitude Classification Examination used by Air Service Section of the U. S. Army; to five of the standard respiratory tests used by the Royal Air Force in England, and to a careful overhaul by a neurologist, internist, ophthalmologist and otologist. The clinical examinations showed thirty-one of these aviators to be stale or physically below par.

In England, in the Royal Air Force, under the guidance of Lieut.-Colonel Martin Flack[1] [2] a set of simple physiologic tests was devised to indicate subjects who were likely to suffer from discomforts in the air, such as headache, giddiness, fainting, nausea, vomiting, pressure in the head, blood rushing to the temples, palpitation of the heart, etc., symptoms which might be due to lack of proper oxygenation of the blood and likely to render the man unfit for flying.

The tests grew in number with experience and the application of them was extended to detect flying stress and fatigue. More recently Flack has stated that he believes them to be of use in determining the physical efficiency of an individual. He emphasizes that these tests are not designed to supplant the work of the clinician in any way, and when a man is reported as physically unfit on these tests it does not mean that the work of the physician is finished but that it is beginning.

If the subject does not come up to standards then the neurologist, cardiologist or general physician will find that something is wrong with him. The tests, it is believed, give indications for such overhaul.

Altitude and Physical Efficiency Tests Used in the Royal Air Force in England. In a complete physiologic examination seven distinct sets of observations are made upon the pilot. These include (1) the response of the pulse to a standard exercise, (2) time the breath is held in seconds after a full expiration and full inspiration, (3) time the breath is held after the standard exercise, (4) vital capacity, (5) extrarespiratory reserve as represented by the factor respiration rate multiplied by ventilation per minute divided by the vital capacity, (6) expiratory force and (7) the "fatigue" test. The value of the tests depends on all being carried out in the same way on all occasions.

The technic and interpretations of five of the tests may be summarized as follows:

1. In holding the breath the seated subject is instructed to expire once as deeply as possible then inspire fully and hold the breath as long as possible. The subject is watched to determine the degree of suffusion and color of the face. The reason for giving up is carefully noted. It is claimed that the breath-holding shows whether there is "oxygen want" and thereby whether the individual is likely to do well at high altitudes. If dizziness, blurred vision, etc., occur under forty seconds the candidate is debarred from flying. Good pilots manage sixty seconds, and it is maintained that all should be able to hold a minimum, in three times, of forty-five seconds.

[1] Lancet, 1919, i, 210.

[2] Anderson: The Medical and Surgical Aspects of Aviation, London, Oxford Press, 1919, p. 55.

2. In measuring the vital capacity the subject is asked to fill his chest and blow hard through a meter, taking precautions against overblowing the meter. The minimum vital capacity is fixed at 3000 c.c. It appears that no account is taken of the size of the man. It is maintained that a capacity below 3400 c.c. and inability to hold the breath for more than forty-five seconds contra-indicates high flying.

3. Bazett,[3] who formulated the respiratory reserve factor, suggested that men with a large vital capacity, a low consumption of air per minute and a slow respiratory rate tolerate high altitudes better than others. He found that the average figure for the good type of flyer is 24.1, for the bad 46.3 and for the uncertain 36.8. A figure of 30 has been taken as the standard, those above this being relatively bad for high altitudes.

4. For the determination of the expiratory force a U-tube manometer, filled with mercury, is used. The subject is asked to blow the column steadily as high as possible and not to swing it up by the momentum of the mercury. It is believed that this is a measure of fitness and of the tone of the abdominal wall. The average normal is about 105 mm. Hg. It was found that pilots suffering from flying stress can often only blow 40 mm. If the test is about 80 the pilot is considered suitable for only low flying, and if much below is probably in need of a rest from flying altogether.

5. The fatigue test is another with the U-tube manometer. The subject is asked to empty the lungs, take a deep breath, blow the mercury to the height of 40 mm. and hold it there without breathing for as long as possible. According to one hypothesis the test is an indication of the tone of the respiratory center. The average normal time of many cases is fifty seconds. Below forty seconds is considered unsatisfactory and indicates that probably the subject is fit only for limited flying or is in need of a rest.

It is not claimed that each test is capable of rigid application but that it is the combination of the tests that is important.

Altitude Classification Examination. The altitude test for the classification of aviators that has been used by the U. S. Army is described in the *Manual of the Medical Research Laboratory* (p. 215). In this test the aviator rebreathes for a period of twenty-five to thirty minutes through the Henderson rebreathing apparatus 52 liters of air from which the carbon dioxide of the expired air is removed by an absorbent. As the oxygen gradually and progressively decreases the subject is under observation by a physiologist, psychologist and clinician. The physiologist determines the rate and volume per minute of breathing, the pulse frequency and the systolic and diastolic arterial pressures. The psychologist records changes in

[3] Report of the Air Medical Investigation Committee, London, 1918, No. 6, p. 7.

attention and motor coördination until the subject reaches the point of complete inefficiency or until the clinician finds that the condition of the circulation makes prologation of the test undesirable. A few subjects exhaust the oxygen to 6 per cent. or a little lower, many reach 7 per cent., while poor subjects may become mentally inefficient or faint at considerably higher percentages, 9 to 12. A majority of all men examined gave the first physiologic evidences of compensation to the reduction in oxygen at between 16 and 14 per cent. of oxygen.

Our data for the 128 aviators have been examined by statistical methods and these are summarized in Table I:

TABLE I.

	No. of cases.	Arithmetical mean.	Probable error.	Correlation with oxygen.	Correlation with oxygen consumption rate.
Final oxygen percentage . .	128	7.59	± .07		
Length of run in minutes . .	128	24.15	± .14	−.51 ±.04	
Vital capacity in liters . . .	128	4.33	± .36	−.06 ±.06	.20 ±.06
Breath held in seconds . . .	127	67.84	±1.22	−.18 ±.06	−.03 ±.06
"Fatigue" test in seconds . .	122	52.20	± .84	−.12 ±.06	.13 ±.06
Expiratory force in Hg. mm. .	123	123.01	±1.82	−.11 ±.06	.10 ±.06
Extra respiratory reserve factor	126	40.55	± .78	.025 ±.06	

The averages as determined in England by the examination of healthy pilots in the Royal Air Force were: Vital capacity, 3800 c.c.; breath-hold, sixty-six seconds; expiratory force, 110 mm.; "fatigue" test, breath-holding while sustaining by blowing a column of mercury at 40 mm., fifty-two seconds. It will be seen that our American group averaged above the English group in vital capacity, expiratory force and breath-holding, while in the "fatigue" test the two groups were the same. In the American group there were 31 men found to be stale or physically below par by clinical examiners.

The Relation of the Ability to Hold the Breath and the Endurance of Low Oxygen. If the time the breath can be held should prove to be an index of ability to respond to the influence of low oxygen it would serve as a simple means of classifying aviators for altitude flying.

Flack has stated his opinion of the breath-holding test as follows: "The test was originally designed to show whether there was 'oxygen want,' and I still believe the test does show the subject who would suffer from 'oxygen want.' From my experience I found that people who were likely to suffer from 'oxygen want' would give up after a very short time in holding the breath and would almost invariably return an abnormal answer. A normal answer would be that the subject 'had to give up,' 'felt he would burst;'

an abnormal answer that 'the blood rushed to his head,' 'things became blurred,' etc."

We have determined that the coefficient of correlation between the time the breath was held and the lowest percentage of oxygen tolerated by 127 men was only -0.18 ± 0.06. This no doubt indicates that the compensation to a gradually decreasing oxygen supply is dependent upon other factors that exert a more profound influence than conditions that obtain during breath-holding and that the power to hold the breath is at the best of only minor importance as a measure of ability to endure low oxygen.

The average time for holding the breath was sixty-eight seconds, the longest time was one hundred and twenty-eight seconds and the shortest thirty seconds.

There were ten men who managed to hold their breath only forty-five seconds or less, the minimum allowed by the English standard, and of these six remained fairly efficient down to 7.5 per cent. of oxygen, one even reached 6 per cent. Four of the men failed between 9.8 and 8.4 per cent. oxygen.

Two groups of breath-holding cases of 13 and 12 each illustrate well the wide range in ability to compensation to low oxygen. There were 13 men who managed to hold the breath between sixty and sixty-five seconds, of these 2 became inefficient in the rebreathing altitude test before reaching 9 per cent. of oxygen, 3 did not reach 8 per cent., 4 failed between 8 and 7 per cent., while the last 4 held on to between 7 and 6 per cent. The group of 12 that held the breath for from seventy to seventy-five seconds became inefficient as follows: 2 before reaching 9 per cent., 3 between 9 and 8 per cent., 3 between 8 and 7 per cent. and 4 between 7 and 6 per cent. of oxygen. It should be noted that these two groups show almost identical distribution in spite of the fact that one group could hold the breath longer than the other.

There were two aviators who fainted at 11.3 and 11.1 per cent. of oxygen. The first, who held his breath ninety-one seconds, was suffering from ethmoiditis and was not fit; the other who held his breath for fifty-nine seconds and reported breathlessness at moderate altitude was found to be stale by the neurologist.

Two other cases are of interest because of early failure in the rebreathing test. The first held his breath ninety-nine seconds but showed a circulatory failure at 10.7 per cent. oxygen. He was found to be physically fit by the clinician but had never flown higher than an altitude of 10,000 feet. The next man held his breath sixty-eight seconds and became inefficient at 10.3 per cent. of oxygen. He was a heavy smoker and complained of being tired after flights at more than moderate altitudes.

There were 12 men who managed to hold the breath for from one hundred to one hundred and twenty-eight seconds, and these,

with one exception, who reached 8.3 per cent., remained efficient to 8 or less per cent. of oxygen.

The correlation of breath-holding with the rate of oxygen consumption was only -0.03 ± 0.06. An analysis of the comparison of these two conditions fails to bring out as close relationship as the ability to hold the breath and the percentage of oxygen reached.

If, as we believe, the rebreathing low-oxygen examination gives satisfactory evidence as to how well a man compensates to low oxygen and high altitudes, then our data indicate that the breath-holding test alone would not suffice as a means for grading men for altitude flights.

Vital Capacity and Low Oxygen. In the Royal Air Force all candidates with a vital capacity below 3000 c.c. are rejected and all below 3400 c.c. are viewed with suspicion. Should a person require a large volume of air per minute it is evident that he may find a large vital capacity useful. In this group of 128 men when seated the average volume of air breathed a minute was 6.7 liters, and when under the influence of a low oxygen of 7.6 per cent. it was 11 liters or there was an increase of 4.3 liters in the total lung ventilation each minute. The vast majority of men when breathing air that contains from 8.5 to 6 per cent. of oxygen inspire at each breath from 600 to 1250 c.c., while their normal volume per breath of normal atmospheric air is between 360 and 640 c.c.[4] We have found a few men when under the influence of 7 or 6 per cent. oxygen who breathed 2000 to 2400 c.c. of air per breath. It is obvious that a man of small chest might be limited to rapid rather than deep breathing in order to secure sufficient ventilation of the lungs when at altitudes comparable to such oxygen tensions as these.

Among the 128 men the vital capacity of the chest averaged 4330 c.c., the smallest was 3090 c.c. and the largest 6620 c.c. The coefficient of correlation between vital capacity and compensation to a gradually decreasing supply of oxygen was exceedingly small, only -0.06 ± 0.06. This suggests that vital capacity when taken alone is almost a negligible factor in the process of making the compensations necessary to supply the oxygen needed by the tissues during exposure to a decrease in oxygen that is comparable to ascending in altitude at the rate of approximately 1000 feet per minute.

There were 5 men among our group of 128 who had a vital capacity of 3400 c.c. or less. They responded to the low oxygen altitude test as follows: (1) Capacity 3090 c.c. endured to 8.5 per cent. of oxygen; (2) 3180 c.c. reached 8 per cent.; (3) 3200 c.c. reached 8.9 per cent.; (4) with a capacity of 3380 c.c. went to 8.4 per cent. and (5) 3400 c.c. remained efficient to 7.6 per cent. of oxygen. These

[4] Schneider: Jour. Am. Med. Assn., 1918, lxxi, 1386.

men reacted as well to oxygen want as many men of greater vital capacity. They did not, however, reach the very low oxygen of some of our cases. Two men with a vital capacity of only 3900 c.c. compensated well to 6 and 6.2 per cent. oxygen.

The 4 men who became inefficient early at 11.3, 11.1, 10.7 and 10.3 per cent. oxygen, percentages that are tolerated well by the vast majority of men, had vital capacities of 4680 c.c., 3900 c.c. 4800 c.c. and 3830 c.c. respectively.

The man who had the largest vital capacity, 6620 c.c., became completely inefficient at 9.4 per cent. oxygen and would have fainted had he not been restored to air immediately.

It appears from the data cited above that the vital capacity when taken alone does not give reliable evidence as to a subject's ability to respond to low oxygen and altitudes. Our experience unfortunately does not include men who at the same time had a small vital capacity and a limited ability to hold the breath.

The Expiratory Force in Relation to Low Oxygen. Unquestionably the expiratory force test is a measure of the power of the abdominal and other expiratory muscles. That the strength of these muscles should be of importance in making the necessary responses for providing oxygen from an atmosphere deficient in this gas does not appear a necessary or even likely correlation. Our data gave a coefficient of correlation for the relationship between the expiratory force and compensation to low oxygen of -0.11 ± 0.06. This is slightly above the correlation between vital capacity and low oxygen and not equal to that between the power to hold the breath and low oxygen. All are too low to be significant.

The coefficient of correlation has been calculated for 120 cases for the relationship between expiratory force and the power to hold the breath and vital capacity. The correlation for expiratory force and the breath-hold was 0.48 ± 0.05, which is a fairly high and quite significant coefficient of correlation. The correlation between expiratory force and vital capacity was 0.24 ± 0.06, which presents a decidedly lesser degree of correlation, but which, nevertheless, is considerably higher than our correlations for these tests with the low oxygen compensation.

Among our group of cases subjected to the low oxygen altitude test there were three men who gave only 70 mm. in the expiratory force test. They compensated to low oxygen down to 8.4, 6.3 and 6 per cent. respectively. On the other hand the 4 men who made a poor showing in the low oxygen test, failing at 11.3, 11.1, 10.7 and 10.3 per cent. of oxygen, registered 140, 178, 88 and 110 mm. respectively in the expiratory force test. Not one of them was below 80 mm., the minimum for normal. These cases here cited are all exceptional, but they clearly show why the coefficient of correlation for expiratory force and low oxygen compensation is so decidedly low.

"Fatigue" Test. This is a form of breath-holding in which the subject by expiratory effort sustains a column of mercury at 40 mm. during the period that he holds his breath. It requires a considerable amount of effort, and therefore, for the majority of men, shortens the period that the breath can be held. Since the test is a modified breath-holding, it was to be expected, as was proved, that its coefficient of correlation with compensation to low oxygen, which was -0.12 ± 0.06, would be about equal to that for the breath-holding test.

Our men in the "fatigue" test averaged 52.2 seconds. The highest record was ninety-seven seconds, made by a man who compensated down to 7.9 per cent. of oxygen. The minimum record of twenty-three seconds was made by a man who compensated well to an extremely low oxygen, 6 per cent.

Six men who reacted poorly to the rebreathing low oxygen test may be cited to further show the lack of correlation of these tests. They failed at the following percentages of oxygen: 11.3, 11.1, 10.7, 10.3, 10 and 9.9. Their respective "fatigue" tests were: 61, 36, 32, 63, 42 and 45 seconds.

The Extra Respiratory Reserve Factor. For 126 of our men the coefficient of correlation for this reserve factor and compensation to low oxygen was surprisingly low, only 0.025 ± 0.06. According to Bazett[5] a low figure for the reserve factor, under 30, indicates that the man is a good type for high altitude flying; such a man should therefore compensate well to low oxygen. Among our subjects there were many striking exceptions. One man with a reserve factor of 41 compensated to 5.7 per cent. oxygen, another with a factor of 40 reached 6.2 per cent. oxygen and a third with a factor of 45 remained efficient to 6.5 per cent. oxygen.

There were 52 of 126 cases who had an extra reserve factor of less than 30. These men compensated to low oxygen as follows: 17 to between 6 and 7 per cent., 24 to between 7 and 8 per cent., 6 to between 8 and 9 per cent., 4 to between 9 and 10 per cent. and one to only 11.3 per cent. oxygen. The average low oxygen reached by our 128 cases was 7.6 per cent. Of this group of 52, with a low figure for the extra reserve factor, 11 failed to reach 8 per cent. oxygen, and therefore could not be classed high in compensation to low oxygen and altitude.

It appears from the above data that any one of the five respiratory tests when taken alone does not give a reliable index as to how well a man may compensate to altitude and low oxygen.

In Table II are given the data for 7 cases of early failure in the rebreathing low oxygen test. It should be noted that two of these cases stand well in each of the respiratory tests and that the others only fail to fulfill the English standards in one or two of the tests,

[5] Loc. cit.

the extra reserve factor and the "fatigue" test. The combination of the respiratory tests does not appear to single out men incapable of compensating to low oxygen any better than did the individual tests.

TABLE II.

No.	Inefficient at oxygen, per cent.	Vital capacity, c.c.	Breath held, seconds.	Expiratory force, mm. Hg.	"Fatigue" test, seconds.	Extra reserve factor.
1. . . .	9.4	6620	55	138	55	18.9
2. . . .	9.9	3950	60	122	45	32.8
3. . . .	10.0	4220	52	96	42	36.5
4. . . .	10.3	3830	68	110	63	35.0
5. . . .	10.7	4800	99	88	32	37.2
6. . . .	11.1	3900	59	178	36	33.5
7. . . .	11.3	4680	91	140	61	24.0

A Comparison of the Tests and Clinical Findings. Among the men considered in this paper there were 31 who were found to be below par by clinical departments of the laboratory. Each man was examined by an internist, neurologist, ophthalmologist and ear, nose and throat specialist. We shall now briefly show how these men responded to the several respiratory tests.

The Rebreathing Low Oxygen Examination as a Test of Physical Fitness. There were many incidents observed among aviators that seemed to indicate that the man who had "gone stale" was very sensitive to low oxygen and particularly liable to syncope when flying. In the laboratory we have seen men with temporary indispositions, such as may follow a bad cold, recent illness, lack of sleep, alcoholic excess, etc., do poorly in the rebreathing examination who at some other time when feeling fit had compensated very well. In view of these occasional findings the reactions of the 31 stale or ailing men was not what might have been expected. They compensated to low oxygen as follows: 11 to as low as between 5.5 and 7 per cent., 12 to between 7 and 8 per cent., 7 to between 8 and 9 per cent. and one to 9.9 per cent. oxygen. From this data it appears that among men who are physically below par some may react very well to the action of low oxygen, as judged by their physiologic and psychologic responses and efficiency.

The rebreathing low oxygen test was perfected to determine the ability of the human organism to respond to the decreasing oxygen tensions of high altitude. Some men compensate well, others inadequately and others not at all. The test should be employed for searching out those unfit for flying by reason of inability to respond to altitude, and also for approximating the altitudes safely tolerated. Physical fitness it appears must be measured by other tests.

Physical Fitness and the Simple Respiratory Test. The determinations for the 31 temporarily unfit men are tabulated below:

Breath-hold.		Expiratory force.	
30 to 39 seconds	= 1	80 to 89 mm.	= 1
40 to 49 seconds	= 0	90 to 99 mm.	= 1
50 to 59 seconds	= 4	100 to 109 mm.	= 3
60 to 69 seconds	= 9	110 to 119 mm.	= 10
70 to 79 seconds	= 5	120 to 129 mm.	= 5
80 to 89 seconds	= 8	130 to 139 mm.	= 3
90 to 99 seconds	= 2	140 to 149 mm.	= 2
100 to 109 seconds	= 1	150 to 159 mm.	= 0
110 to 119 seconds	= 1	160 to 169 mm.	= 1
		170 to 179 mm.	= 1
Total	= 31	180 to 189 mm.	= 4
		Total . . .	= 31

Vital capacity.		"Fatigue" test.	
3000 to 3499 c.c.	= 1	20 to 29 seconds	= 1
3500 to 3999 c.c.	= 7	30 to 39 seconds	= 5
4000 to 4499 c.c.	= 11	40 to 49 seconds	= 7
4500 to 4999 c.c.	= 5	50 to 59 seconds	= 12
5000 to 5499 c.c.	= 6	60 to 69 seconds	= 2
5500 to 5999 c.c.	= 0	70 to 79 seconds	= 4
6000 to 6499 c.c.	= 1	80 to 89 seconds	= 0
Total . . .	= 31	Total . . .	= 31

Extra respiratory reserve factor.

10 to 19	= 3
20 to 29	= 11
30 to 39	= 5
40 to 49	= 3
50 to 59	= 3
60 to 69	= 0
70 to 79	= 2
Total .	= 27

Only 1 of these unfit men held his breath less than forty-five seconds, the minimum for normal established in England; 1 had a vital capacity of 3180 c.c., which was below the minimum of 3400 c.c.; 6 held the breath in the "fatigue" test for less than the forty seconds, the minimum for normal, while 14 showed up unusually well in the extra reserve factor and only 8 made a very poor record, and not 1 was below the minimum normal allowed in the expiratory force test. There were 11 cases that did not fall below the minimum for normal in any one of these five respiratory tests while only 2 men fell below the minimum normal in three of the tests.

In the breath-hold 17 were above the average, 68 seconds; in the "fatigue" test 14 were above the average, fifty-two seconds; in the respiratory force 14 above 123 mm., the average, and 15 had a vital capacity greater than the average, 4330 c.c.

Our experience with these respiratory tests is similar to that of White[6] in the U. S. Base Hospital No. 6 in France, in which he tried

[6] Am. Jour. Med. Sc., 1920, clix, 866.

out the value of the breath-holding, vital capacity, expiratory force and the "fatigue" test on convalescent gassed cases. He concluded that they were tests of the stability of the nervous system, rather than of cardiac and pulmonary condition.

Birley[7] working with English aviators at the front found that pilots and observers whose condition warranted their transfer to England for a rest preserved a comparatively high degree of physical fitness as judged by the tests. He believes that they afford valuable information in assessing temperament and susceptibility and reaction to shock. He found that they did not prove useful in searching out psychopaths, individuals, who never feel confident in the air and sooner or later reach the hospital with well developed anxiety neurosis.

Practice Effects. In order to determine the effects of practice and experience on the five respiratory tests 7 men were asked to repeat the tests every day for a week. The results obtained with 5 of the men are given in Table III. The data for the 2 men not recorded here show similar variations. It should be noted that the men followed their regular daily routine of living during the period and that no environmental conditions, habits of living or sickness were recorded that might account for the variations and improvement. Each man coöperated to the best of his ability, so we may conclude that the differences recorded are the results of practice and the fortunes of the details of coördination and position.

In breath-holding not a man held his breath the same length of time in any two trials. Each showed a considerable amount of variation. Six of the men improved the time of the hold with practice as much as eighteen to fifty-one seconds. Holding the breath requires will power, if a man determines to hold the breath until discomfort is profound, it can be done or he may give up with the first feeling of effort. Private Ha. by effort increased his power of holding the breath from thirty-one seconds, which is below the minimum for normal, to sixty-four seconds, which was within four seconds of the average for our group of 128 aviators.

In the "fatigue" test, which is also a breath-holding test, some skill is required in sustaining the column of mercury at 40 mm. and a proper set of the lips will appreciably ease the performance. All of our men also showed improvement with practice in this test. Sergeant L. R. increased his performance each day, so that on the fifth day he held sixty-three seconds longer than on the first day.

The expiratory force test practice effect shows improvement in five of the seven men. One subject, whose complete data are not here given, raised the mercury column to 132 mm. on the first day and to 218 mm. on the seventh day.

[7] Report of the Air Medical Investigation Committee, London, 1918, No. 3, p. 25.

TABLE III. PRACTICE EFFECT.

	1st day.	2d day.	3d day.	4th day.	5th day.	6th day.
SERG. L. R.						
Breath-hold in seconds	71	95	100	80	122	
Expiratory force in millimeters	50	68	72	68	160	
Vital capacity in cubic centimeters	5560	5400	5000	5200	5700	
"Fatigue" in seconds	30	50	55	64	93	
CORP. K.						
Breath-hold in seconds	65	67	63	58	76	
Expiratory force in millimeters	80	92	138	88	78	
Vital capacity in cubic centimeters	4300	4180	4100	4400	4100	
"Fatigue" in seconds	36	55	52	51	55	
PRIVATE I.						
Breath-hold in seconds	50	60	49	43	75	
Expiratory force, millimeters	120	140	180	116	160	
Vital capacity in cubic centimeters	4000	3900	3720	4000	3860	
"Fatigue" in seconds	..	46	55	40	63	
PRIVATE Ha.						
Breath-hold in seconds	31	57	64	59	56	
Expiratory force in millimeters	134	140	130	120	136	
Vital capacity in centimeters	4170	4190	4000	3970	4500	
"Fatigue" in seconds	40	48	65	54	49	
PRIVATE Hu.						
Breath-hold in seconds	62	65	85	81	75	82
Expiratory force in millimeters	60	54	70	96	94	104
Vital capacity in cubic centimeters	3700	3890	3650	3660	3760	3690
"Fatigue" in seconds	51	51	63	53	53	67

The data on vital capacity do not show that practice gives an increase in the record.

Conclusions and Summary. Certain criticisms may be offered against the simple respiratory tests. They require too much voluntary attention and hearty coöperation on the part of the patient. The results are not capable of physiologic interpretation unless they represent the best effort the patient can put into each test. Indifferent subject and listless observer both vitiate the results. If the patient wishes a vacation, knowing that a poor showing in the tests indicates fatigue and need of a rest, he can easily imitate the "all-in" man. The tests are in some respects psychologic, since if a man determines to hold his breath until

discomfort is pronounced it can be done or he may give up with the first feeling of effort.

To sustain the mercury column in the "fatigue" test requires some skill and a proper set of the lips may ease the performance so much that twenty and more seconds are added to the length of the hold. The expiratory force test, if well done, requires great effort and the height of the blow often depends upon the ability to co-ordinate the contraction of chest and abdominal muscles.

The coefficients of correlation for the power of breath-holding, vital capacity, "fatigue" test, expiratory force and extra respiratory reserve factor, with compensation to low oxygen, were found to be of such low value that the simple respiratory tests could not be accepted as aids in determining fitness for high altitude flying.

The degree of physical fitness it appears as shown by an examination of 31 temporarily unfit men cannot be measured either by the simple respiratory tests or by the low oxygen of the rebreathing test.

Seven men were able to improve their records in the respiratory tests by practice.

SACCULAR ANEURYSM OF THE DESCENDING THORACIC AORTA, WITH DIRECT RUPTURE INTO THE LOWER LOBE OF THE LEFT LUNG AND THE LEFT PLEURAL CAVITY:

THE REPORT OF A CASE AND REMARKS ON RUPTURE AND HEMOPTYSIS IN AORTIC ANEURYSM.

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At this time when quantitative and functional studies are so much in vogue, one hesitates on first thought to present a morphologic study. Nevertheless, the writer is of the opinion that such studies still hold a definite and valuable place in clinical medicine. In spite of the fact that our viewpoint has been expanded to incorporate the newer ideas of functional pathology, the clinician must still depend in a large part upon a thorough knowledge of gross pathology for his interpretation of physical findings. With this idea in mind it appears that unusual and instructive cases should be conscientiously studied and recorded, notwithstanding the fact that some of the work will doubtless be a repetition of what has been done.

The medical literature of aneurysm in all its phases is already astonishingly extensive and varied, and associated with its scientific

development and collaboration are innumerable illustrious names in the annals of medicine.

The present paper was stimulated by a case which recently occurred in the Medical Service of the University of California Hospital, which the writer unfortunately did not see antemortem. The necropsy findings, however, directed my attention to the subject of aneurysm of the descending thoracic aorta, with special reference to rupture into pulmonary structures. The following report is interesting in the light of the necropsy findings:

Case History. The patient, J. S., a white man, aged fifty years, American, was admitted to the University of California Hospital on March 29, 1920, at 7 P.M. and died on March 31, 1920, at 2.30 P.M. On admission his temperature was 38.4° C., respiration 36 and pulse 104. He complained of "cough and weakness," which was of four years' duration, and of a pain in the left lower chest.

Family History. Father died at sixty-eight of unknown cause; mother died at seventy-two of old age; two brothers killed; one sister died at twenty-seven during childbirth. Patient married at twenty-seven and was divorced four years later; no children.

Past History. Born in Colorado and lived in California from thirty to fifty. He has been employed as a miner and steel-miller.

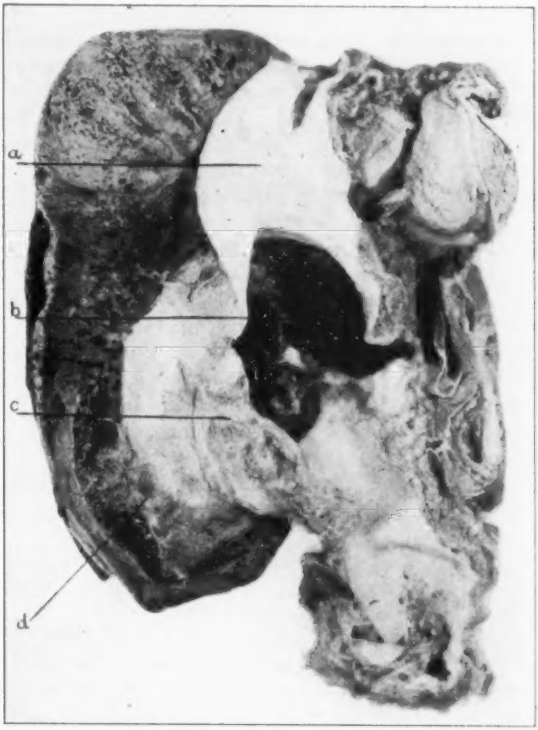
Diseases. Does not remember having childhood diseases. Influenza at twenty-five and again at forty-eight. He had pneumonia at thirty-four, and Neisser infection without known complications at eighteen and forty; lues denied.

Accidents. He is said to have fractured skull at twenty-three.

Habits. He had used alcohol steadily all his adult life and had been a heavy smoker.

Present Illness. Four years ago the patient had a sharp pain in the right lower chest, which increased in intensity during coughing and deep breathing. Since then he states that he catches cold very readily and has had a chronic cough; he has been below par most of the time. About four months ago the patient had a severe cold, with a chill and fever, but was not sick enough to be in bed. Since then he has improved slightly but has not felt as well as formerly. Four days ago patient was again seized with chills and fever, and yesterday morning on arising he felt a sharp pain in the lower left chest; this pain was more marked on deep breathing and coughing and was relieved by lying on the affected side. Although he has had some cough for the last four years, this has been more severe during the last three months. Recently he has had considerable sputum, mostly of the colorless, stringy, mucous variety but never blood-tinged. There is no history of hemoptysis nor night-sweats. His best weight is 180 pounds; average weight 170 pounds; present weight 158 pounds. He has had some shortness of breath off and on for the last three years, but this has been especially noticeable during the last three months.

Physical Examination. Well-developed and nourished man, lying on the left side, coughing frequently and expectorating a thin sputum mixed with a small amount of light greenish, mucopurulent material. Patient complains of sharp pain in the left lower chest. Head, ears and nose are negative. Eyes: Bilateral pterygium on the corneæ; pupils regular and equal and reacting actively to light and accommodation; extra-ocular movements well performed;



Specimen removed at autopsy; posterior view. *a*, descending thoracic aorta; *b*, opening into the aneurysmal sac; *c*, posterior wall of the aneurysm; *d*, lower lobe of the left lung.

fundi normal. Mouth: The teeth are absent; tongue heavily coated, symmetrical and freely movable. Tonsils: Atrophic; pharynx is injected. Neck: Negative and the thyroid is not palpable. Chest: Conforms to the moderate pigeon-shaped variety. Right side is more prominent than the left anteriorly. In the upper thoracic region the spine is slightly deviated to the right. The right supraclavicular area is depressed. There is a

marked impairment of the percussion note in the left axilla which extends forward, fusing with the relative cardiac dulness and extending posteriorly to the left base. Over this area tactile fremitus is absent. There is a friction rub high in the left axilla. Anteriorly below the left clavicle the breath sounds are harsh and loud. Grocco's triangle of dulness is made out at the right base along the spine. Heart: P. M. I. is best heard at the fifth rib in the left parasternal line; the R. C. D. is displaced markedly to the right; the right border of the R. C. D. is made out 5.5 cm. to the right of the midsternal line in the fifth right interspace. There is a loud, blowing systolic murmur heard best at the aortic area. This murmur can be heard as far up as the first interspace and as low down as the third interspace on the right side. There is no diastolic shock over the sternum to be made out. The rhythm is regular; the rate is 108 per minute. Pulse shows good tension, rapid rise and fall, and the vessel wall is not palpable. Blood-pressure is $\frac{110}{80}$. Abdomen has normal contour and is rather resistant to deep palpation; no definite tenderness nor masses are made out. Genitalia are negative. Deep reflexes are equal and active throughout. The mental state is apparently normal. Blood examination: R. B. C., 3,800,000; W. B. C., 13,000; differential count (100 cells): P. M. N., 81; S. M., 14; L. M., 5; P. M. E., 0; P. M. B., 0. Urine examination: Sp. gr., 1.026; cloudy; acid; albumin, F. P. T.; sugar, 0; sediment, many urates and a few pus cells, but no casts. Impression: Tuberculous pleurisy, with effusion at the left base and displacement of the heart to the right.

March 31, 1920, at 9 A.M. Patient complaining of pain in the left side especially on cough. Side strapped with adhesive. Patient coughed considerably.

March 31. At 2.30 P.M. adhesive strapping was removed in preparation for thoracentesis. Patient continued coughing in paroxysms. He expectorated a small amount of a foamy, mucoid sputum and complained of pain in the left lower chest. Suddenly he began bringing up a small amount of blood, at the same time he became very restless and sat up straight in bed, and after four or five gasping spells he became unconscious and cyanotic, and respiration ceased rather sharply. The whole amount of blood expectorated did not exceed 30 or 40 c.c. The heart-beat was audible for a moment or two after respiration ceased.

Wassermann (on blood serum postmortem) was triple plus.

Fluoroscopic and roentgen-ray examinations had not been done because the patient was too ill to move.

Clinical impression as to the cause of death: Massive pulmonary hemorrhage into a bronchus in a case of ulcerative pulmonary tuberculosis.

Postmortem Record of the Pathologic Laboratory. A. 20.59, University of California, performed by Dr. G. Y. Rusk, autopsy one hour after death.

Anatomic Diagnosis. Aneurysm of the aorta, with rupture into the left lower lobe and into the left chest cavity; syphilitic aortitis; dislocation of the heart to the right apex in the midline; chronic local pleurisy about the aneurysm; pulmonary syphilis (?); chronic infarct in the spleen; acute anemia; chronic aortic valvulitis, with adhesions between the segments leading to slight stenosis.

Remains of a muscular, well-nourished male adult of normal stature. Rigor mortis absent. Body heat well retained. No superficial lymphadenopathies. The pupils are circular and equal. Moderate conjunctivitis is present. The left chest appears slightly fuller than the right.

On making the usual median incision the bodily fats are normally preserved and of normal color. The voluntary muscles are somewhat pale and the rib cartilages are somewhat more than normally calcified. On opening the left chest cavity there is a gush of blood-stained serum. The posterior surface of the sternum is negative. The left chest cavity contains an abundance of clotted blood and separated serum.

The heart is displaced to the right, so that the apex lies in the midline. The chest cavity is free from adhesions or fluid.

The right lung is voluminous and shows an average amount of pigmentation. It is hypercrepitant on palpation throughout. On section it is negative except for a moderate grade of diffuse emphysema.

The left lung, while somewhat compressed by the great amount of fluid in the pleural cavity, still is somewhat enlarged. The upper lobe is diffusely hypercrepitant, the lower lobe posteriorly superficially shows ragged point of rupture situated about one-third of the distance above the diaphragm on its posteromesial aspect. Adjacent to this, and extending to what subsequently proved to be an aneurysmal sac, is an area of diffuse opaque pleural thickening, but without adhesions. The tissues of the lower lobe, especially posteriorly, are suffused with hemorrhage which gradually diminishes in intensity toward the more anterior portions. The lung was removed together with the entire aorta, which will be described below. On section through the lower lobe there is found an area of irregular fibrosis extending in a wedge-shaped manner from near the root to the periphery through the center of the lower lobe. This area contains several patches of necrotic material and the process strongly suggests scarring associated with gummata.

The pericardial cavity contains about 30 c.c. of clear, fluid, serous transudate. The heart is of normal size considering the general development of the individual; it weighs 320 grams. The epicardial fat is normal. The relative size of the chambers appears normal. The endothelium of all the cavities, including the valves, except the aorta, appears normal. The myocardium is of normal thickness. The muscle is contracted. No areas of fibrosis were

observed. The aortic valve shows the right posterior segments to be adherent and the line of juncture thickened, pulled foreward, separating the region of attachment of the segments for about 1 cm. from the aortic wall. On either side of this line of attachment there is a diffuse, gradual, lessened thickening of the adherent cusps, which extends to the region of the corpus on the posterior segment and throughout the whole of the right segment. This deformity appears to have led to a slight stenosis. The aorta just above the aortic cusps shows some irregular, soft, slightly yellowish superficial patches of atheroma, and in addition presents a number of areas, with irregular depressed, stellate creases of syphilitic aortitis. This condition of specific aortitis occurs with remarkable frequency throughout the whole length of the aorta. In the mid-thoracic region the left wall of the aorta presents a large opening, 8 x 10 cm., where it opens widely into an aneurysmal sac, approximately 8 cm. deep. The base of the aneurysm is formed by a thrombotic layer, which is supported on the thinned-out wall. The point of actual rupture into the bronchi is not determined until after fixation of the specimen.

The esophagus is normal, except that it was distinctly misplaced to the left by the aneurysmal dilatation.

The vertebra also as yet shows no destruction.

The spleen is moderately increased in size and somewhat softened. On section the pulp is pale, the Malpighian bodies are fairly numerous and only moderately distinct on the pale background. Corresponding to a small puckered scar in the cortex is a fibrous tissue thickening which extends about 3 mm. into the spleen, apparently the result of quite an old infarct.

The adrenals appear normal.

The kidneys appear normal.

The remainder of the urinogenital apparatus appears normal.

The pancreas shows a slight fibrosis in its distal half.

The liver appears normal except for slight palor.

The mesenteric and retroperitoneal lymph nodes are negative.

The muscosa of the gastro-intestinal tract appears normal.

Occurrence. Aneurysms of the descending thoracic aorta are the least common of all the aortic aneurysms, occurring only a little more than half as frequently as abdominal aneurysms. In 64 cases of aneurysms of the aorta among 2200 autopsies at the Johns Hopkins Hospital only 3 involved the descending thoracic aorta (Osler[1]). Since the publication of Osler's monograph[2] on this subject, in 1903, little has been added to our clinical knowledge of descending thoracic aneurysm; however, since then much scientific advance has been made as to the causal relationship of syphilis to vascular disease and aneurysm formation, refinements in the roentgen-ray study have been outlined and numerous methods of therapy have been proposed and advocated.

Diagnostic Difficulties. Osler pointed out that in general there were three groups of descending thoracic aneurysm based on clinical observation and physical findings liable to present serious difficulties in the diagnosis, namely: (1) Cases which present symptoms only and no physical signs or the signs are not characteristic; (2) cases in which the symptoms and signs suggest malignant growth; (3) cases in which there are obscure and puzzling chest symptoms suggestive neither of aneurysm nor tumor (the above case falls into the third group).

The features which warrant classification of this case in the third group are based on the following data: (1) The comparative latency of all clinical symptoms except the history of pain of three months' duration in the left lower chest; (2) the cough was never characteristic or typical of thoracic aneurysm; (3) the striking yet misleading physical signs indicating fluid at the left base; (4) the absence of hemoptysis except as a terminal event.

Anatomical Considerations. Owing to the protected and deep position of the descending thoracic aorta, extending from the sixth to the twelfth thoracic vertebra, aneurysms of this portion are frequently silent. It will be recalled that the descending arch passes backward and downward to the left of the trachea, behind the root of the left lung, to the left anterior aspect of the thoracic vertebra. As it passes downward the esophagus and thoracic duct lie on its right. The left pleura and lung lie to the left and anteriorly. The descending arch of the aorta and the thoracic aorta below are held firmly in place by the intercostal branches which are given off from the aorta. In view of the existence of these special anatomic relations distinctive clinical manifestations may be produced which offer evidence of deep-seated thoracic disease. There are, in general, two large groups of structures which appear to be involved in aneurysms of the descending thoracic aorta, and when involved may give clinical evidence of intrathoracic disease. From the clinical standpoint the first group is the most common, although many special examples of involvement of structures in the second group are found.

Group I. 1. Spine, vertebra and spinal nerves. 2. Lung, pleura and bronchi. 3. Trachea and esophagus.

Group II. 1. Pericardium and heart. 2. Other great thoracic vessels, including pulmonary arteries, veins, etc. 3. Stomach. 4. Thoracic duct. 5. Diaphragm.

It is not my intention to review the symptoms and signs produced by encroachment upon or rupture into all of the above structures but rather to point out some of the facts of interest in regard to ruptured descending thoracic aneurysms into the pulmonary structures and particularly into the lungs.

Rupture of Aneurysms in General. It is a well-known fact, particularly to pathologists who perform large numbers of postmortem

examinations on medicolegal cases, that ruptured aneurysms stand high in the list of causes of sudden death. As long ago as 1895, Draper,[3] in this country, published a paper entitled "Sudden Death by Rupture of Thoracic Aneurysm Previously Unrecognized," which emphasizes this point.

In reference to the cause of death from aneurysm, Hare and Holder[4] state "that death occurs as a result either from rupture of the aneurysmal sac, from pressure of the sac upon important nerves and bloodvessels or from secondary changes which take place in these tissues and in other vital organs as a direct or indirect result of such pressure." Arnold[5] made a study of the cause of death in aneurysms of the aorta which do not rupture. He found in a large series of aortic aneurysms of all types 110 of the descending aorta, and of these 15 per cent. were unruptured at death, whereas 66 per cent. were found ruptured. From his statistics it also appears that descending aortic aneurysms are slightly more liable to rupture than those in other portions of the aorta.

Oswald Browne's figures indicate definitely that the most common termination of aneurysms of the descending thoracic aorta is rupture into the left pleural cavity. In his series of 17 cases in which 14 ruptured, 7 instances of rupture into the left pleural cavity occurred. The incidence of rupture at other points was as follows: Right pleural cavity, 2 cases; left bronchus, 1 case; esophagus, 3 cases; subserous tissue, 1 case.

Wilson[6] collected from the literature 75 cases of descending thoracic aneurysm, 53 of which had ruptured. In these ruptured cases he found that 13 cases had ruptured into the left pleura, 1 into the right pleura, 6 into the left lung, 16 into the left bronchus, 2 into the trachea, 2 into the pericardium and 9 into the esophagus. It was stated that in 2 instances rupture had occurred into the thoracic cavity, in 1 instance into the abdominal cavity, and once into the neck. In the remaining 22 cases rupture did not occur. Erosion of the vertebræ occurred in 26 instances, whereas an external tumor was encountered in only 6 of the 75 cases. In this series the clinical diagnosis was missed in 50 per cent. of the cases. In Osler's series of 14 cases, rupture into the pleura occurred 3 times, whereas in Wooley's[7] recent series of 9 ruptured aneurysms of all types 2 ruptured into the left pleural cavity. The foregoing figures emphasize the marked tendency that aneurysms of the descending thoracic aorta have for rupturing into the pulmonary structures, and particularly into the left pleural cavity.

Hemoptysis. Clarke,[8] in 1905, reported a remarkable case of thoracic aneurysm which had come under his observation. The case was unusual in that the patient had a series of 16 copious hemorrhages, and in a period of seven and a half weeks lost a total of fourteen pints of blood before exitus occurred with hemorrhage. In the last moments of life during the fatal hemorrhage the physical

signs of fluid at the right base were made out. The autopsy revealed a saccular aneurysm of the ascending arch of the aorta projecting into and occupying a great portion of the upper lobe of the right lung, with rupture of the aneurysm into this lobe and extensive hemorrhage into the right pleural cavity. The striking feature presented by this case is the possibility of copious non-lethal hemorrhage in cases of thoracic aneurysm.

In the same paper Clarke refers to a case reported by Johnson[9] which appears very similar to the case I report above. Johnson's patient had long-standing symptoms of chronic pleurisy, but no history of hemorrhage until the fatal one. Aneurysm was not suspected, but at autopsy one was found of the descending aorta involving the lower left lobe of the lung. The aneurysmal walls were only one-quarter inch thick, composed of fibrin, and the lung and pleura were indurated.

Clarke concludes from his study of aneurysms in reference to hemoptysis "that hemoptysis is a common fatal termination in thoracic aneurysm, a very large hemorrhage may occur in this disease, without causing death of the patient, and that occasionally a patient may have one or more large hemoptyses, but finally die from some other complication of the aneurysm. The point of bleeding may be from rupture into the trachea or bronchi and may be stopped by the opening being plugged with fibrin or it may occur from involvement of the lung tissue itself. In the latter case it is probable that the small bronchioles open into the wall of the sac, but are compressed by it, that they normally remain closed, or are covered with fibrin. On exertion of moving, either the fibrin shifts its position or the straining of the coughing opens the ends of the small bronchi and the blood leaks out. When the patient again becomes quiet, either naturally or by means of narcotics the original condition is resumed and bleeding is temporarily arrested."

The foregoing statement appears to be a fairly reasonable explanation of the intermittent nature of hemoptysis in some of these cases.

Hall[10] in an able paper on the subject of intrathoracic aneurysm groups the mechanisms of pulmonary hemorrhage in these cases under three heads: (1) Direct hemorrhage, that is, when there is a leak from the aneurysmal sac into the air passages; (2) indirect hemorrhage, that is, when the hemorrhage is the result of pressure either on the air passages, the bloodvessels or the lung tissue itself; (3) hemorrhage secondary to cardiac disease with engorgement, of the pulmonary circulation.

Remarks on Other Symptoms—Pain, Cough and Dyspnea. In my case presented above pain played the conspicuous role in the symptomatology. Hewlett and Clarke[11] have pointed out in a small series of descending thoracic aneurysms that pain was the prominent symptom. They found it was usually of extraordinary severity,

constant, subject to nocturnal exacerbations and resistant to all forms of medication. In general, pain is of three kinds: (1) Anginal, (2) that due to pressure, and (3) neuralgic.

It is a well-known fact that aneurysm often produces the clinical picture of angina pectoris,[12] and, further, that obscure and deep-seated thoracic pains of all variations are sometimes produced by pressure of intrathoracic aneurysmal tumors. In the neuralgic type pain reaches its maximum intensity and persists when the aneurysmal sac erodes the spine.

The mechanism of pain in thoracic aneurysm has been explained in various ways. Increased tension of the walls of the aorta can of itself become a cause of pain by stretching of the delicate nerves which run in the walls of the aorta producing a neuritis. Oliver[13] states that digitalis administered in suspected cases often augments pain in the chest, since by improving the force of contraction of the left ventricle and by constricting the peripheral arteries it raises arterial tension. Other factors in the production of pain include, of course, that caused by pressure on adjacent structures and the coexisting inflammation.

Cough and dyspnea are practically always constant features of involvement of the aortic arch, but are less constant in aneurysm of the descending portion of the aorta. In Osler's 14 cases these symptoms were present in 10 instances. Bronchorrhea and bronchiectasis result at times from pressure on the main bronchus.

Summary. A case of descending thoracic aneurysm is presented which had ruptured directly into the left lower lobe and left pleural cavity. The physical signs were misleading and the clinical diagnosis was incorrect. It is probable that if a roentgen-ray study had been possible it would have aided materially in determining the true nature of the pathologic process. Rupture into pulmonary structures of descending thoracic aneurysms is one of the most frequent occurrences, particularly rupture into the left pleural cavity, less commonly into both lung and pleural cavity. Hemoptysis must be regarded as a symptom of thoracic aneurysm as well as a symptom of other thoracic disease, such as tuberculosis, mitral stenosis and other mediastinal tumors. It may be frequent and persistent before a fatal hemorrhage occurs.

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SILVER SALVARSAN IN THE TREATMENT OF SYPHILIS.*

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Through the courtesy of Ehrlich's distinguished pupil and successor, Professor Kolle, early in November, 1919, Colonel Earl H. Bruns, chief surgeon, A. F. in G., received 1000 ampoules of silver salvarsan from the George Speyer Haus Laboratories, Frankfürt, Germany. Colonel Bruns turned this preparation over to Major Robert W. Kerr, Medical Corps, the Commanding Officer of the Base Hospital (now Station Hospital), A. F. in G., Coblenz, Germany, with instructions concerning its use which he had obtained personally from Professor Kolle. The first results seemed favorable and its further use was decided upon. Additional

* Weichbrodt, Knauer, Seoli-Bonn and Gennerich: Ztschr. f. Aerztliche Fortbildung, Georg Speyer Haus, Frankfürt.

supplies of this preparation were obtained through medical department procurement.

Since that time over 800 patients have been treated with silver salvarsan and mercury, more than 6000 injections having been given at the Base Hospital and Convalescent Hospital by or under the direction of the following officers: Majors Carter and Flynn; Captains Kimbrough, Raycroft and Moore; Lieutenants Cowen, Thomas, Blackburn, Bourbon and myself. The laboratory work in connection with the Venereal Clinic has been done by Major Gentzkow, Lieutenant McNeil and Lieutenant Elmendorf.

Composition and Description of Silver Salvarsan. Kolle[1] states that silver salvarsan contains 22.4 per cent. arsenic and 14.1 per cent. silver. Bauer[2] says that the silver in silver salvarsan is not present in the oxide or colloid form, but in a complex combination that may be considered half colloids, on the boundary between colloids and crystalloids.

He advances the theory, based on different experiments, that these semicolloids act as colloids in the system. He states that in silver salvarsan, neosalvarsan and old salvarsan the relative chemotherapeutic coefficient is silver salvarsan 1 to 25, neosalvarsan 1 to 10, old salvarsan 1 to 10. He further states that the arsenic component is materially decreased in silver salvarsan owing to the combination with the antisyphilitic silver component. His diffusion experiments make it seem probable that silver salvarsan is hydrolized in the body and set free as true colloids. A single dose of two-tenths (0.2) gm. of silver salvarsan contains 0.0254 silver and 0.043 of arsenic.

Silver salvarsan is prepared in the Ehrlich Laboratories at Frankfürt and the powder is placed in ampoules in the following doses: One-tenth (0.1) gm., fifteen hundredths (0.15) gm., two-tenths (0.2) gm., three-tenths (0.3) gm. The powder is grayish black and in solution takes on an ichthyol brown color.

Characteristics of Spoiled Silver Salvarsan. Silver salvarsan in the original ampoules keeps for an unlimited time so long as it is not damaged. Small cracks in the glass permitting the entrance of air cause silver salvarsan to become decomposed and thereby made poisonous. The decomposition is not so easily discernible in looking at an ampoule of the silver salvarsan while in powder form as when placed in a solution.

If the silver salvarsan has deteriorated the powder is darker in color and does not change to an ichthyol brown color when placed in solution, but takes on an opalescence of pronounced cloudiness, or it floats around on the surface of the water in black particles in which the undissolved silver salvarsan is recognized by the naked eye when the solution is held to the light.

Silver Salvarsan as a Spirocheticide. Kolle and Ritz[3] state that silver salvarsan is to be considered a true combined preparation

containing two chemotherapeutically effective components, silver having a catalytic effect on the salvarsan molecule. They further state that it has been experimentally proved that arsenobenzol is a direct spirocheticide, because of anchoring of the arsenic in the spirochetic plasma. Many experiments, especially those showing the slow disappearance of the spirochetæ after the administration of this drug, incline to the opinion that silver acts as a restricting agent on the multiplication of spirochetæ. The action of the silver in silver salvarsan is successful in preventing an increase of spirochetæ because of the specific affinity of the salvarsan to the spirochetæ, the silver with the whole molecule of the silver salvarsan is anchored fast to the spirochetæ of the syphilitic tissues. For this reason the combination of the silver with the salvarsan is of special chemical therapeutic value. The silver salvarsan acts also on the spirochetæ within the syphilitic tissue as a combination remedy in the sense that this term was used by Ehrlich.

In a series of experiments they have shown that in rabbits the curative dose of the metal silver, or its salts, is one-hundredth (0.01) gm. to two-hundredths (0.02) gm. per kilogram of the rabbit's weight, the toxic dose for rabbits being six-hundredths (0.06) gm. to seven-hundredths (0.07) gm. The spirochetæ disappear slowly but surely from the infected rabbit. The hard chancre softens and finally disappears. Not only does colloidal silver but also organic and inorganic silver salts combined with albumin influence the manifestation of syphilis and the spirochetæ. The effect on the spirochetæ and its manifestations is slower with all silver salts than with arsenobenzol, but the former can be given in larger doses with less toxic effect. Spirochetæ disappear more slowly with colloidal silver than with non-colloidal compounds. The primary manifestations of syphilis in experimental animals disappear in from three to five weeks after therapeutic healing doses of silver compounds. Animal experimentation finds silver salvarsan twice as effective as salvarsan (606) and three times as effective as neosalvarsan (914). Kolle further states that silver salvarsan is old salvarsan in active form plus silver and that 0.25 silver salvarsan equals 0.4 old salvarsan.

Technic of Administration of Silver Salvarsan. Bruhns and Lowenberg[4] use one-tenth (0.1) gm. of silver salvarsan dissolved in 20 c.c. of freshly distilled sterilized water; in the larger doses 30 to 40 c.c. of freshly distilled sterilized water.

Kerl[5] uses 6 c.c. of freshly distilled water to every one-tenth (0.1) gm. of silver salvarsan. Delbanco and Zimmern[6] make a solution with from 10 to 20 c.c. according to quantity of preparation. Lenzmann[7] uses 20 to 40 c.c.; four-tenths (0.4) per cent. solution of sodium chloride. Schoenfeld and Birnbaum[8] prefer 60 to 80 c.c. of normal sodium chloride (C. P.) solution. Kolle[1] recom-

mends 10 c.c. of distilled water to each one-tenth (0.1) gm. Dreyfus[9] states that we should use only redistilled sterilized water from the Jena glass apparatus, avoiding the use of any metal that would come in contact with the solution except the platinum needle.

Kerl[5] prefers a modified Arzt Schramek syringe. Lenzmann[7] uses a Lieberg syringe. Birnbaum[8] uses the Schreibus glass syringe. Kolle[1] suggests Wechselmann's apparatus.

Practically all the above-mentioned authorities emphasize the importance of giving the solution very slowly. Bruhns and Lowenberg[4] state that the least time required for each injection should be at least two minutes. Kolle[1] calls particular attention to the irritating effect of silver salvarsan on the tissues and states that caution should be used so that injury to the inner wall of the vein does not occur and that great care is used in seeing that the needle is in the vein properly before administering the solution.

The technic used at the Station Hospital and Convalescent Hospital is as follows:

The water is distilled the day previous to its use. The distilled water is boiled on the day of the administration of the silver salvarsan. The water used is at room temperature. The silver salvarsan ampoules are immersed in 95 per cent. of alcohol, 20 c.c. of the sterilized distilled water are placed in a 60 c.c. medicine glass and the contents of the ampoule containing the silver salvarsan are dropped into the glass containing the distilled water. The silver salvarsan powder floats around on the surface of the water until it is completely dissolved, which takes approximately one minute. The solution now takes on an ichthyol brown color. The contents of the medicine glass are now drawn up into a 30 c.c. Luer syringe. Just prior to the insertion of the needle the operator dries same with a piece of sterile gauze in order to prevent the solution from coming into contact with the tissues. After the needle is introduced into the vein enough blood is withdrawn to fill the syringe. By this means we are positive of the needle being in the lumen of the vein, and, according to Kolle, the toxicity of silver salvarsan is immediately reduced by the addition of albumin or serum. The injection of the solution is made slowly, requiring approximately one minute. The needle is withdrawn quickly and the operator raises the patient's arm and uses marked pressure at the site of the injection in order to prevent extravasation of the fluid back into the tissues.

Dosage. Galewsky[11] considers small doses of silver salvarsan necessary in the treatment of syphilis. He commences it with five-hundredths (0.05) gm. for anemic women, otherwise one-tenth (0.1) gm.; increases the dose every four or five days to a final maximum dose of three-tenths (0.3) gm. to men and twenty-five-hundredths (0.25) gm. for women. Total given by him to

men in the course of treatment is 1.8 gm. and for women 1.5 gm. He ordinarily gives eight to fifteen injections of silver salvarsan in the first course of treatment for primary seronegative syphilis and four to six injections in after-treatment. In order to avoid what he terms spirochetæ fever in virulent secondary stage of syphilis, he gives a first dose of five-hundredths (0.05) gm. and second dose of fifteen-hundredths (0.15) gm.

Dreyfus[9] states that no fixed total dose has been found as yet. He has given as high as 3 or 4 gms. to a patient in from six to ten weeks without after-effects.

Schoenfeld and Birnbaum[8] state that they use for the first two or three doses for men one-tenth (0.1) to two-tenths (0.2) gm., and for women one-tenth (0.1) gm. to fifteen-hundredths (0.15) gm. For the next five or six doses in strong men they give three-tenths (0.3) gm. to thirty-five hundredths (0.35) gm. and for strong women two-tenths (0.2) gm. to twenty-five-hundredths (0.25) gm. They follow this treatment with three or four doses at six-day intervals, giving men twenty-five-hundredths (0.25) gm. and women two-tenths (0.2) gm. They state that the average total dose of 2.5 to 2.75 gm. for men and 2 gm. to 2.5 gm. for women should be given in ten to twelve injections.

Bruhns and Lowenberg[4] give the following course of treatment: Twelve injections of silver salvarsan with three or four days' interval. For the first dose they give one-tenth (0.1) gm. followed by five doses of two-tenths (0.2) gm. and this is followed by six doses of twenty-five-hundredths (0.25) gm.

Kerl[5] administers one-tenth (0.1) gm. and two-tenths (0.2) gm. of silver salvarsan on two succeeding days, and after an eight-day interval repeats the treatment until he obtains a negative Wassermann reaction. Later, because of the slow response of Wassermann reaction, he gave one-tenth (0.1) gm., two-tenths (0.2) gm.; two-tenths (0.2) gm. on three successive days and repeated after an eight-day interval.

Delbanco and Zimmern[6] give on first dose five-hundredths (0.05) gm. or one-tenth (0.1) gm. Second dose, one-tenth (0.1) gm. and the next six to ten injections a dosage of two-tenths (0.2) gm. or twenty-five hundredths (0.25) gm. They gave their injections with an interval of from three to five days. They state that silver salvarsan may be given daily without bad results. Boas and Kissmeyer[12] gave only four injections in each treatment with a dosage of fifteen-hundredths (0.15) gm., twenty-hundredths (0.20) gm., and twenty-five-hundredths (0.25) gm. They state that when treatment has been going on for some time there should be a long interval between each dose, at least as much as eight or ten days.

Lenzmann[7] gives at the first dose one-tenth (0.1) gm., and if no bad effects follow he then gives fifteen-hundredths (0.15) gm. on

the third day, on the sixth day two-tenths (0.2) gm., ninth day twenty-five-hundredths (0.25) gm., then four injections of twenty-five-hundredths (0.25) gm. a week apart, and on the following week a dose of three-tenths (0.3) gm. He further states in seronegative primary syphilis five to six injections are sufficient, while in seropositive primary syphilis it requires seven to ten injections, according to the duration of the positive reaction. He states that fresh secondary syphilis up to two or two and a half months' duration requires only one treatment of ten to twelve injections if the serum reaction turns negative four weeks after taking up treatment. Where this was not the case the patient with secondary syphilis received a second treatment six weeks after the first, consisting of eight to ten injections at five-day intervals.

Rille and Frühwald[13] give in single doses from two-tenths (0.2) gm. to four-tenths (0.4) gm. of silver salvarsan at intervals of from three to seven days, giving in all six to eight injections.

Kolle[14] states that we must try to make the therapy so effective in the nine to eighteen injections, intervals from two to five days, that in perhaps 90 per cent. or more of the primary or early secondary cases we may expect complete sterilization. He advises beginning the treatment with one or two injections of one-tenth (0.1) gm. and increasing the dosage to two-tenths (0.2) gm. for women, with twenty-five-hundredths (0.25) gm. for men as a maximum dose, with an interval of four days. He says that we should never give more than 2 gm. of silver salvarsan in a month.

Major Kerr appointed a Board of Medical Officers consisting of Major H. P. Carter, Captains Kimbrough and Raycroft to investigate and recommend a treatment for the cure of syphilis with silver salvarsan. This Board recommended the following treatment:

An interval of seven days between each dose in each course of treatment.

Treatment to consist of four courses of silver salvarsan and gray oil.

In the first course of treatment the first dose to be fifteen-hundredths (0.15) gm. of silver salvarsan.

Second dose to be two- enths (0.2) gm. of silver salvarsan.

And each of the remaining five doses of the first course to be three-tenths (0.3) gm. of silver salvarsan.

At the end of the first course of treatment a Wassermann blood test and then thirty days' rest.

In the second course of treatment three-tenths (0.3) gm. silver salvarsan for each dose, with seven-day intervals, then two and a half months' rest. Course to consist of seven doses.

The third course same as the second with ninety days' rest.

The fourth course same as second or third course.

In conjunction with and at the same time of each injection of

silver salvarsan give eight-hundredths (0.08) gm. gray oil, intramuscularly.

A Wassermann blood test was recommended after each course and a spinal fluid examination after the second course. During the second year of the disease perform every three months a Wassermann blood test and lumbar puncture with a complete serological examination of the spinal fluid. If at any time the Wassermann becomes positive treatment will be renewed. If at the end of the twenty-fourth month the Wassermann blood test and spinal fluid are negative the case is considered cured. This treatment was later somewhat modified by making an interval of four days between injections during the first course.

Primary Syphilis. Hoffman[15] states that with one complete intensive course of treatment with mercury and salvarsan in primary syphilis we get a complete cure. Hoffmann, Neisser and Scholz[15] claim a successful abortive cure of syphilis should be attained in from 80 to 100 per cent. of all cases, *provided the patient presents himself for treatment in the prepositive Wassermann period.* Fabry[16] states that it is generally admitted now that in primary lues sterilization is obtained prior to the positive Wassermann period in 100 per cent. of all cases. Galewsky[15] says that in all cases of early syphilis showing a positive dark field and negative Wassermann they continued to show a negative Wassermann throughout their treatment with silver salvarsan and during one year of observation following this.

It is believed we have reached the point where we should differentiate between primary and secondary syphilis by the Wassermann, and consider syphilis with primary lesions, primary syphilis, until Wassermann is positive, and then call it secondary syphilis. One should be extremely cautious in stating that a cure has been attained in any stage of syphilis, and observation of a patient, both from a clinical and serological standpoint, for a period of many years, appears to be essential before drawing any definite conclusion. To tell a patient that even in early syphilis he will be cured may give him a false security that in the end may do him an injustice as well as others. It would seem a better plan to tell the patient that some authors claim a cure, but that a cure is not at all certain. However, this much is certain, as a rule, syphilis, like tuberculosis, can be controlled if the patient follows instructions.

In a study of our syphilitic registers there were found 133 early cases where a diagnosis was made by a dark-field examination. These cases were divided into periods of from one to five, five to ten, ten to fifteen, fifteen to twenty, twenty to twenty-five, twenty-five to thirty and over thirty days, in which, according to patient's statement, he had noticed the primary lesion. The cases in question have been under treatment anywhere from four to ten months.

The following table shows those cases which have always had a negative Wassermann and those which at some time during treatment the Wassermann became plus minus, plus or double plus:

No. of cases.	Days lesion existed.	Always negative.	Became plus minus, single plus or double plus while under treatment.	Approximate percentage always negative.	Approximate percentage run plus minus, single plus or double plus.
27	1 to 5	22	5	81	18
43	6 to 10	29	14	63	32
17	11 to 15	13	4	76	23
7	16 to 20	3	4	42	57
6	21 to 25	4	2	66	33
8	25 to 30	3	5	34	62
25	over 30	9	16	36	64
133		83	50	62	37

In the above small number of tabulated cases, all of which were diagnosed by a dark-field examination, 83 ran a negative Wassermann throughout their treatment, and 50 cases became plus minus, single plus or double plus during treatment. *In all the cases in this series which gave other than a negative Wassermann, such result was obtained a few days after beginning treatment, and this would lead one to believe that the case when starting treatment was on the verge of, or actually in, the secondary stage.* It must also be understood that the information regarding the *time the primary lesion had been observed* was necessarily *obtained from the patient*, many of whom stated that the lesion was about the size of a lead pencil when first noticed. Sometimes the *information* given by the patient was *not dependable* because his statement might be what he deemed best for his individual interest, having in mind the disciplinary action necessary by existing orders in case he failed to take the prophylactic treatment required at the time of exposure. Upon requestioning many of these patients about the duration of the primary lesion, explaining the reason such information was desired and assuring them the truth would not lead to disciplinary measures, I found in many cases the soldier had noticed the primary lesion much longer than stated in his original questionnaire. Unfortunately, at the time the re-investigation was made with reference to the duration of the local lesion, in most of the cases where the table shows a primary lesion existed anywhere between one and twenty days and Wassermann became plus minus, plus or double plus, the soldier had left the American forces in Germany.

It is held that *if* the period of the *primary lesion* could be *definitely stated* in the above tabulated cases, where the *lesion existed less than fifteen days* they would always run a negative Wassermann. It will be of interest to follow this series of cases many years in order to determine if there has been an apparent abortive cure of

syphilis. Certainly in this type of case only can we expect an abortive cure.

Wassermann Reaction in Secondary Syphilis. Hahn[17] states that in cases of seropositive lues he usually obtains a provisonally permanent negative Wassermann with ten injections of silver salvarsan. In such cases he gives two injections a week, one of two-tenths (0.2) gm. and one of three-tenths (0.3) gm. Galewsky[15] says that in a great number of cases of positive Wassermanns after an injection of silver salvarsan the Wassermann remained negative and no symptoms showed up later. However, in these cases too short a time had elapsed to speak of permanent results. He also states there were isolated cases in which notwithstanding an application of salvarsan and mercury the Wassermann remained permanently positive. Sellei[18] states that it is impossible to arrive at a definite conclusion from a survey of the cases so far treated with reference to the Wassermann. In two cases of secondary syphilis a reversion of the positive Wassermann was obtained within two or three weeks; however, he had a great number of cases where the Wassermann did not become negative until five or six weeks had passed. Hahn[19] states that after twelve injections of silver salvarsan the Wassermann was always negative in fresh cases, and nearly always negative in older cases. In those cases in which it was not negative six more injections of silver salvarsan were made without injury to the patient, and in some instances he went beyond that number, reaching twenty-four injections. Fabry[16] states that the reversion of the Wassermann in several cases had not come up to his expectations. In one-half of the cases treated by Hoffmann[15] with ten injections of silver salvarsan the Wassermann reaction remained positive. Kolle[1] is of the opinion that we should obtain a negative Wassermann after twelve injections given as outlined by him under "Dosage" in this article, except in those isolated cases where there appeared to be a Wassermann-fast blood.

Knopf and Sinn,[20] in a series of 30 cases, 14 of which were treated with silver salvarsan alone and 16 with silver salvarsan and mercury, obtained the following results:

THE WASSERMANN BECAME NEGATIVE.

Without Hg, after silver salvarsan, gm.	Cases.	With Hg, after silver salvarsan, gm.	Cases.
0.8	1	0.8	7
1.2	3	1.2	4
1.6	6	1.6	1
1 8	2	2.4	1

The Wassermann remained positive twice without mercury and three times with mercury.

Müller[37] obtained the following serologic results in a series of 73 cases, using silver salvarsan alone:

Blood Wassermann after silver salvarsan.	L.I. 27	L.II. Manifest 27	L.II. Latent 13	L.III. 5	L. Hereditary 1
0.6	8	4	4	1	—
0.9	5	2	—	—	—
1.2	6	7	5	—	—
1.5	5	4	—	1	—
1.8	3	3	2	—	—
2.4	—	6	1	—	—
Total	27	26	13	2	0
Remained plus, p. c.	0	1	0	3	1

At the Station Hospital and Convalescent Hospital in a series of 61 cases of secondary syphilis manifested by a double plus Wassermann and clinical evidence of the disease in the secondary stage, the following negative Wassermann reactions were obtained after each dose of the first or second course of treatment:

First Course of Treatment.

No. of cases.	Doses of silver salvarsan.	Doses of novo-arseno-benzol.	Doses of gray oil.	Gave a negative Wassermann.
2	1	—	1	2
2	2	—	2	2
6	3	—	3	6
9	4	—	4	9
11	5	—	5	11
7	6	—	6	7
10	7	—	7	10
1	1	6	7	1
2	1	6	7	2
50				50

Second Course of Treatment.

3	1	—	1	3
2	2	—	2	2
1	4	—	4	1
2	6	—	6	2
1	—	4	4	1
1	—	5	5	1
1	—	6	6	1
11				11

Our present schedule of treatment provides a rest of one month between first and second course of treatment. A summary relative to Wassermanns in this series of 61 cases may be tabulated as follows: 55 cases received silver salvarsan and gray oil of mercury; 47 of these cases gave a negative Wassermann in the first course, which consisted of seven treatments. The remainder (8 cases) gave a negative Wassermann in second course of seven treatments.

Approximately 83 per cent. gave a negative Wassermann at end of first course, and the remaining 17 per cent. gave a negative Wassermann at the end of second course. Six cases received sometime during their treatment silver salvarsan, novo-arseno-benzol, and gray oil of mercury, three gave a negative Wassermann in first course of treatment and three gave a negative Wassermann in second course of treatment. The number of cases in this series is, of course, too small for any final conclusions; however, it would appear that silver salvarsan has a slight advantage over novo-arseno-benzol relative to reversing the Wassermann.

Our syphilitic registers show 516 patients have completed the first, second or third course of treatment, approximately 70 per cent. of these cases gave a negative Wassermann after first course of treatment, 25 per cent. gave a negative Wassermann after second course of treatment and 5 per cent. gave a negative Wassermann after third course of treatment. In other words the selected cases in a series of 61 with manifestations of secondary syphilis give a higher percentage of negative Wassermanns than these 516 cases. This may possibly be explained by the fact that in our series of 516 cases there are many who received a portion of their treatment with novo-arseno-benzol, others did not take treatment regularly, and still others probably had a latent secondary or tertiary syphilis.

Silver Salvarsan with or without Mercury. Galewsky[11] states that a Wassermann is negative sooner with silver salvarsan than neo-salvarsan, he further prophesies that there will be no more relapses into premature tertiary or premature neurosyphilis. He considers silver salvarsan the best remedy discovered to date, and as a result of two years' experience he prefers straight silver salvarsan to the combination of mercury and salvarsan. He thinks there are fewer after-effects than in any other salvarsan preparation tried.

Bruhns and Lowenberg[4] state that silver salvarsan often works quicker than mercury salvarsan combination.

Hauck[21] believes that the addition of mercury is unnecessary in giving silver salvarsan, he says that owing to the toxic effect it paves the way to salvarsan poisoning.

Nolten[22] states that mercury is superfluous when using silver salvarsan.

Gennerich[23] states that the addition of mercury is unnecessary in giving silver salvarsan. He further states that in seropositive and secondary lues the Wassermann turns negative somewhat sooner with silver salvarsan than with other salvarsan preparations, even in combination with mercury. He recommends mercury only in cases where a third treatment is necessary because of the long time since infection. He says it can be used between the silver salvarsan treatments because it prevents the spirochetæ from recuperating.

Fabry[24] states that one must be extremely careful with mercury and silver salvarsan in combination. He believes you should begin with silver salvarsan and not follow too closely with the mercury.

Von Notthaft[25] thinks that treatment with silver salvarsan and mercury at the same time is a mistake, owing to the toxic effect of mercury on the liver and kidneys. Wechselmann, Pinkus, Scholtz and von Notthaft have given up the use of mercury.

Boas and Kissmeyer[12] use mercury and silver salvarsan in combination. They state that mercury may be superfluous but it does no harm.

Lenz[26] states that he can only support in an approving manner the favorable results reported of silver salvarsan.

Kreibich[27] says that given the same proportion of arsenic, silver salvarsan is superior to old salvarsan, in which connection the inferior toxicity of the former permits a higher proportionate dosage.

Hahn[17] states that the effect of silver salvarsan on syphilis is excellent; he has good results in all stages of syphilis. He had quite a number of patients who did not yield to other treatment but in whom after the administration of silver salvarsan the Wassermann became negative and remained so. He states that in seropositive lues with an average of ten injections of silver salvarsan he was able to obtain a permanent negative Wassermann.

Goldberger[28] states that considering the inferior toxicity of silver salvarsan compared with old salvarsan, and its higher efficiency compared with neosalvarsan, it makes a valuable addition to antisyphilitic remedies. He thinks a combination with mercury appears to be the best treatment.

Sellei[18] states that silver salvarsan operates in a very energetic manner and after a very short time the symptoms completely disappear. He believes the use of silver salvarsan particularly indicated where there is a nephritis present.

Clinical Effects of Silver Salvarsan and Mercury. Kreibich[27] states that the same rapid and intensive effect is obtained on the spirochetæ with silver salvarsan as with old salvarsan (606).

Galewsky[11] states that within twenty-four to twenty-eight hours after an injection of silver salvarsan the spirochetæ are often not to be found in the local lesion.

Bruhns and Lowenberg[4] state that the exanthemata disappear remarkably quickly; the running papules dry up one day following the injection and soon heal.

Lenzmann[7] states that there was a decided influence on the spirochetæ four hours after a dose of one-tenth (0.1) gm. of silver salvarsan, within twelve hours practically no living spirochetæ could be found.

Major Gentzkow and Lieutenant McNeil, in the Laboratory

Service at the Station Hospital, did not find living spirochetæ in the initial lesion twenty-four hours after an injection of silver salvarsan. Lieutenant Elmendorf, of the Convalescent Hospital, states that actively mobile spirochetæ have been found as long as twenty-one hours after an injection of silver salvarsan fifteen hundredths (0.15) gm. plus eight-hundredths (0.08) gr. of gray oil, and that inactive spirochetes were found in the local lesion as long as twenty-six hours after an injection of silver salvarsan and gray oil. The number of spirochetæ present in preparations made after an injection of silver salvarsan and gray oil were invariably greatly reduced. No organisms were found forty-eight hours after the time of injection of silver salvarsan.

The effect of silver salvarsan on all grades of syphilis is favorable. The local manifestations appear to clear up as rapidly as they did under the older salvarsan preparations. There is a decided change in the initial lesion after the first treatment, indurations pass off quickly, glands are reduced in size, exanthemata pale down and the mucous patches and condylomata heal rapidly. The best apparent results obtained by silver salvarsan, as in all cases of salvarsan preparations, were in those showing the ordinary clinical signs of secondary syphilis, with mucous patches in mouth and throat and exanthemata.

Immediate Effects Sometimes Seen after Silver Salvarsan. *Anaphylactoid Symptoms.* Swift (*Jour. Am. Med. Assn.*, 1912), after experimenting with guinea-pigs showed that a serum change took place after the first injection of salvarsan which led to the sensitizing of the animal.

J. Danepz, R.D.L. (*Academie de Science*, 1916) is of opinion that the after-effects of arsenobenzol compounds, alarming in many patients, are caused by a precipitation within the capillaries. According to him this precipitation is caused by the reaction of an antibody with the next injected arsenobenzol. He recommends giving oversensitive patients small preparatory doses.

Kolle, Schlossberger and Leupold,[29] in their experiments with mice showed that intravenous injections of small doses of salvarsan gave certain protection against an absolutely deadly dose twenty-four hours later. Many investigators place the after-effects of salvarsan preparations in the category of anaphylaxis, and insofar as the first injections are concerned, as parallel to primary serum poisoning. For this reason the after-effects manifested soon after the beginning of intravenous salvarsan injections are frequently called anaphylactoid.

Galewsky,[15] speaking of so-called angioneurotical symptoms, states that these symptoms were noticeable immediately after the first injection with some of the patients; with others they only became manifest after subsequent injections, so that it can only be a question of anaphylactoid manifestations after repeated intravenous injections of silver salvarsan. He states the symptoms

were chiefly noticeable in persons strongly alcoholic, or in patients suffering from heart affections.

Hahn[19] says that the anaphylactoid symptom-complex turns up immediately after injection, he rarely came across it and it never became an embarrassing form except in the case of patients where an affection of the meninges was to be presumed.

Friedlaender[30] described cases suggesting to him the idea of anaphylaxis, wherein patients showed a few clonic twitches which were rapidly transformed into a shaking tremor of the whole body, cyanosis and weak pulse. In his opinion in these cases it is a question of Herxheimer reaction and the term anaphylaxis has only been used to account for the clinical similarity of the symptoms with genuine anaphylactoid manifestations.

From the most recent investigations by Schmalt, Giessen and Sachs[30] the presumption appears justified that anaphylaxis is not a chemical reaction of the albuminous substance but a process due to physical causes. These authors, apparently quite independently of one another, come to the same conclusion, viz.: that anaphylaxis can be produced by the incorporation of non-albuminous substances, as for instance carbohydrates, provided colloids only are concerned, but that the true anaphylactic effect immediately disappears if such solutions are first passed through a Berkefeld filter and the filtrate only is injected, or if the emulsion is considerably heated before injection so that the colloidal solutions are transformed into chemical solutions. They come to the conclusion that in intermittent silver salvarsan treatment the danger of anaphylactoid manifestations comes into question at the time of the first injection, and that for the repeated use of it it would be advisable to commence each fresh series with a small dose in order to first overcome the oversensitiveness.

Angioneurotic Symptoms. Lenzmann states that a strong concentration of silver salvarsan leads to angioneurotic symptoms.

Delbanco and Zimmern[6] state that patients having a tendency to angioneurotic symptoms should be given injections very slowly.

Schoenfeld and Birnbaum[8] speak of angioneurotic symptoms which are sometimes followed by collapse.

Kolle[14] states that angioneurotical manifestations are, as a rule, due to the repeated injections of too concentrated doses of the remedy, and in most cases they can be avoided. He further states that in treating patients attention is called to the necessity of good nourishment and to the avoidance of excesses of any kind. By following these directions the angioneurotic symptom-complex can most certainly be avoided. But it should be pointed out that the said symptom-complex does not in any circumstances offer any apprehension, because so far no single case of death due to silver salvarsan has been recorded, in spite of more than 100,000 injections.

Hahn[19] states that the 1-per-cent. solution as used by him renders it possible to prevent the cropping up of angioneurotic symptoms.

Goldberger[28] states that he never saw the so-called angioneurotical symptom-complex as described by Pinkus,[28] nor the vasomotor signs as were observed by Galewsky[28] and Sellei.

The angioneurotic symptoms as described by many authors are: vomiting, dizziness, pain in the back, edema of lips and face.

Spirochetæ Fever. In primary and secondary cases it is no uncommon occurrence to observe a rise of temperature after the first injection, which should be interpreted as spirochetæ fever; this does not constitute a contra-indication against a continuation of the treatment. If there is a higher rise of temperature after the second or third injection, or if the high temperature is continued over a longer period, further treatment must be interrupted for a certain time until the conditions of the patient have resumed their normal state.

Fabry[32] states that spirochetæ fever is caused by the decrease in the number of spirochetæ, usually after injections with silver salvarsan in secondary lues. Should salvarsan anaphylaxis set in, increase the interval or decrease the dose.

Our experience has been that we get a reaction after the first dose of any arsenobenzol preparation in late primary or early secondary syphilis. We have always interpreted this as being caused by the spirocheticidal effect of any arsenobenzol preparation on the spirochetæ, thereby suddenly throwing a protein substance in the circulation and producing the so-called spirochetæ fever. This may be interpreted as angioneurotic symptom-com plex, or anaphylactoid reaction. We have never seen a reaction following silver salvarsan that we considered alarming.

Neurorelapses. Ehrlich and Gennerich[34] have said that monorecidives are caused by the local spreading of unsterilized spirochetæ. Kolle[1] thinks that we should never be alarmed over neurorelapses, he states there has never been a case of neurorecidive which was later reported as cerebrospinal syphilis. Kreiblich[27] and Sellei[18] have not seen cases of nervous relapses after silver salvarsan. Galewsky[11] and Sinn[35] each report 1 case. In more than 800 cases our records do not show a case of neurorelapse.

Periphlebitis. This rarely occurs and is always due to faulty technic, the extravasation of the solution into the tissues at the site of injection, or trauma to intima of the vein. An abscess at site of injection has occurred only once to my knowledge in our complete series. In the out-patient clinic of this hospital there are given nearly three hundred injections on the morning of the day our out-patients are treated.

Effect on Later Manifestations of Syphilis. Weichbrodt, Knauer, Seoli-Bonn and Gennerich[14] state that the spinal fluid is strongly influenced by silver salvarsan.

Dreyfus[9] says that silver salvarsan can have after-effects more

frequently than neosalvarsan; however, he reports good results in syphilitic diseases of the nervous system. The best results were obtained in the early stage of the disease. He states that the subjective symptoms disappeared after a few injections and the objective symptoms in one or two weeks.

Kolle[14] speaks of silver having been used for many years in the treatment of nervous diseases with apparently good results.

Hahn[17] states that he obtained good results in cerebral syphilis and remarkable effects in tabes.

Galewsky[15] also obtained good results with silver salvarsan in nervous syphilis.

Goldberger[28] is impressed with silver salvarsan and thinks that further investigations should be made with this drug.

In 2 cases in which Friedlaender[30] has used silver salvarsan he was led to believe that salvarsan or neosalvarsan is preferable to silver salvarsan in nervous syphilis.

Under the direction of Major Flynn, Captain Kimbrough has obtained the spinal fluid in 19 cases of patients under treatment in this hospital, after having finished their third course of treatment. The laboratory examination was made by Major Gentzkow, who reports the Wassermann negative in all these cases with the exception of 2, in which the spinal fluid gave a plus-minus reaction. The two last-mentioned cases had been treated with other arsenobenzol preparations during the first course of their treatment, and in addition they had not received their treatment regularly. In one of these cases the Wassermann was single-plus strong. The patient did not take treatment regularly, there was a lapse of six months between first and second course, and in the first course the patient was given novo-arsenobenzol rather than silver salvarsan. In the other case the Wassermann was plus-minus and the patient was given novo-arsenobenzol in the first course rather than silver salvarsan.

Captain Price, Chief of the Eye, Ear, Nose and Throat Service, has treated 8 cases of syphilitic iritis which were given silver salvarsan as outlined heretofore in this article. He states that he was greatly impressed with the results obtained by this drug. He wished to emphasize in particular one case which yielded surprisingly rapidly to treatment. The patient in question was almost entirely blind from interstitial keratitis on his admission to the hospital. He further states that the results obtained in this case with seven months' treatment with silver salvarsan were such as ordinarily he could not have expected before seventeen months.

Argyria. We have not been able to find any case of argyria reported in the literature, as the result of silver-salvarsan treatment. Our cases have not developed any such manifestations.

Poison after Administration of Silver Salvarsan. Foulerton[36] states it appears that the results characteristic of poisoning by

arsenobenzol compounds may be produced by the action of arsenic alone. But in view of the serious damage to the liver and kidney tissues in experimental poisoning with ortho-amido-phenol it is impossible to ignore the probability that the toxic action of the arsenobenzol drugs may be influenced to some extent by the benzine constituent.

So-called arsenic poisoning from arsenobenzol preparations may be classed as acute, subacute and chronic. In a series of more than 6000 injections of silver salvarsan in patients who are either still under treatment or who have been under treatment with silver salvarsan in conjunction with mercury, there have been only two cases of so-called arsenical poisoning which could be attributed to silver salvarsan. In all the other cases of poisoning at this hospital the patients received novo-arsenobenzol. One of of these cases received three doses of silver salvarsan. First dose was fifteen-hundredths (0.15) gm. silver salvarsan, eight-hundredths (0.08) gr. gray oil. Second dose (six days later) two-tenths (0.2) gm. silver salvarsan, eight-hundredths (0.08) gr. gray oil. Third dose (four days later) three-tenths (0.03) gm. silver salvarsan, eight-hundredths (0.08) gr. gray oil. On the same day following the third dose of silver salvarsan and gray oil the patient suffered from headache, chills and dizziness, vomited twice and complained of pain in the epigastric region after the injection of silver salvarsan that day, three days later he developed sore-throat, diffuse erythema over the entire body, face edematous and red, a temperature of 101.4 and slight jaundice. The patient's urine was positive for albumin from the day following the second dose of silver salvarsan until fifteen days later. The other case received the first course of treatment. On the day following the last dose patient states the tips of his fingers and toes felt numb, skin became red in patches, which was quickly followed by a diffuse erythema, urine showed albumin and four days later early evidence of jaundice.

Albuminuria. Müller[37] states albumin in the urine was never noticed in his cases. Many authorities consider nephritis as a contra-indication to the administration of salvarsan, even in syphilitic nephritis. Sellei states that silver salvarsan had a favorable influence on the kidney in three cases where there was a nephritis in combination with the syphilis.

About 4 per cent. of our cases show albumin in their urine sometime during their course of treatment. They may be tabulated according to the number of doses of silver salvarsan and mercury as follows:

No. of cases.	No. of doses of silver salvarsan and mercury.	No. of cases.	No. of doses of silver salvarsan and mercury.
1	1	2	6
2	2	8	7
3	3	6	During 2d course.
4	4	3	During 3d course.
7	5		

In about one-half of the cases the albumin cleared up under further treatment and as would be expected these cases were those who showed albumin in the early part of the treatment. On the contrary, in those cases in which the albumin appeared during the latter part of first course or later, there was a tendency for the albumin to persist until further treatment was discontinued.

The confusing factor in cases showing albumin in their urine while under treatment for syphilis is the fact that we may be dealing with a transient or toxic albuminuria, from various causes, *i. e.*, syphilis, mercury, any arsenobenzol preparation or the various organic or infectious diseases.

In view the fact that many writers in using silver salvarsan alone do not speak of an albuminuria, it would indicate that in some of our cases in which this condition presented itself in the latter part of the disease it may have been due to mercury.

It is hoped that a report on albumin occurring during treatment may be made at a later date.

Summary. 1. Silver salvarsan is the strongest spirocheticide as well as being the least toxic of all arsenobenzol preparations, according to results obtained from animal experimentation, that has yet been introduced, and nothing has so far developed in its clinical application to contradict these observations.

2. Silver salvarsan deteriorates rapidly when exposed to the air, and this deterioration is recognized best when the silver salvarsan is placed in solution.

3. Technic of administration requires.

(*a*) Strict asepsis.

(*b*) Freshly distilled sterilized water in the proportion of 10 c.c. to each one-tenth (0.1) gm. of silver salvarsan.

(*c*) Silver salvarsan powder must be completely dissolved before administration.

(*d*) Proper precaution to prevent extravasation of the silver salvarsan solution into the surrounding tissues is essential.

(*e*) Slow administration, *i. e.*, not less than one minute.

4. If silver salvarsan is used alone probably the best treatment (based on the results reported in recent literature) is as follows:

Begin the treatment with one-tenth (0.1) gm. of silver salvarsan, increase dosage to two-tenths (0.2) gm. for women and twenty-five-hundredths (0.25) gm. for men as a maximum dose, with an interval of four days between doses, and never give more than 2 gm. in any one month.

5. The results obtained in primary syphilis on the Wassermann reaction are as good, if not better, than with any other arsenobenzol preparation used in combination with mercury.

6. The Wassermann reaction reversed to negative as rapidly in secondary syphilis with mercury and silver salvarsan as in any other arsenobenzol preparation with mercury.

7. Mercury should be given with silver salvarsan in the treatment of syphilis. Whether or not it should be given at the same time or following the silver salvarsan is another question. In military service it is desirable to give the two at the same time.

8. The effect of silver salvarsan on all clinical manifestations of syphilis is decidedly rapid, and appears at least as effective as that of any other arsenobenzol preparation.

9. Alarming effects of silver salvarsan were never seen in any of our cases.

10. Constant vigilance in the administration of all arsenobenzol preparations is essential. Particular attention should be given to patient's weight, a beginning erythema, functional kidney and liver tests.

11. Kolle, Ritz, Galewsky, Hauck and Gennerich appear to be of opinion that silver salvarsan is better than any other salvarsan preparation. Boas, Kissmeyer and Müller seem to think that silver salvarsan is on a par with salvarsan. Dreyfus, Kerl, Schoenfeld, Birnbaum, Bruhns, Lowenberg and Goldberger think that silver salvarsan is better than neosalvarsan. Hoffmann, Knopf, Scholtz and Sinn prefer salvarsan to silver salvarsan. Von Nothhaft says he obtains no better results from silver salvarsan than other salvarsan preparations. Friedlaender, Sellei and Hahn speak of very good results from silver salvarsan; Fabry says it might well be called upon to supplement or supplant neosalvarsan.

Conclusions. 1. Give mercury with silver salvarsan until it has been definitely proved that the mercury is unnecessary.

2. Energetic and intensive silver salvarsan and mercury treatment are indicated in early primary syphilis during the prepositive Wassermann period.

3. Silver salvarsan in so-called abortive treatment of syphilis is not so dangerous as other arsenobenzol preparations.

4. The literature on silver salvarsan and our own experience with this preparation, warrants the further continuation of its use.

5. An excellent field for the further study of these cases and the subject in general is now afforded at the Station and Convalescent Hospitals. It is hoped that the work is just begun, and that by a careful tabulation of the cases now on hand, and the careful observations noted in our syphilitic registers, by the teamwork of the various professional services and with the careful system of follow-up which it is expected to institute, this series of cases alone should in time enable us to draw definite conclusions as to the efficacy of this preparation.

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REVIEWS

SYPHILIS: DIAGNOSIS AND TREATMENT. By LOYD THOMPSON, PH.B., M.D., Hot Springs, Arkansas. Second edition. Pp. 486; 81 engravings and 7 colored plates. Philadelphia, Lea & Febiger, 1920.

IT is a pleasure to review the second edition of Thompson's book, now appearing after a lapse of three years, during which time its authority and value we feel has been thoroughly substantiated. There is not a great deal of change, but what is present is well chosen; for instance, the decline in value of the luetin test called for considerable retraction of its interpretation except in infants, the appreciation of the remote syphilitic manifestations allows of greater amplification in the chapters dealing with them, as is likewise true of the increasing use and dependency of the colloidal gold test, and we consider it wise, as the author has done, to establish the now almost universal custom of speaking of the Spirocheta pallida in preference to its other designations. The literature references are most complete and correct, while the illustrations, with few exceptions, are excellent and well chosen.

A. R.

SURGERY, ITS PRINCIPLES AND PRACTICE. By A. P. C. ASHHURST, A.B., M.D., F.A.C.S.; Associate in Surgery in the University of Pennsylvania; Surgeon to the Episcopal and to the Philadelphia Orthopedic Hospital. Second edition. Pp. 1202; 1129 illustrations and 14 colored plates. Philadelphia: Lea & Febiger, 1920.

THE first edition of this work was written in 1914. Since that time there has been much change in various treatments, conceptions and ideas many of which are due to the experience obtained as a result of the war. This the second edition brings the subject-matter up to date. Some of the old sections have been rewritten entirely. The branch of reconstructive surgery has been assembled into one place rather than being distributed throughout the book as in the first edition.

The chapter on gunshot wounds has been entirely rewritten, as

also have those sections dealing with shock, infected wounds, infections of the fingers and hand, hydrocephalus, carcinoma of the tongue, empyema, and surgery of the pancreas. Seven new colored plates and over one hundred new illustrations have been inserted. By means of judicious curtailing the new matter has all been added with only an increase of 60 pages in the size of the book.

Genito-urinary surgery, gynecology and orthopedics are discussed only so far as they concern the general surgeon. The specialties eye, ear, nose and throat are omitted.

The work is a most excellent one in most every respect. In fact in every respect but one and that is a fault of too much rather than too little in the way of choice and number of illustrations. Many of the illustrations of advanced conditions might better be replaced by earlier stages of the diseases, thus helping more in early diagnosis.

The work is good and the author is to be congratulated.

E. L. E.

NITROUS OXIDE-OXYGEN ANALGESIA AND ANESTHESIA IN NORMAL LABOR AND OPERATIVE OBSTETRICS. By F. H. McMECHAN, M.D., Editor. Pp. 97. Columbus, O.: Hahn & Adair Printing Company, 1920.

THIS distinctive monograph which has been prepared for the National Anesthesia Research Society by a number of anesthetists and obstetricians, who have acted as a Committee of Publication, gives a most comprehensive recapitulation of the modern theories of, ideas concerning, and methods of use of nitrous oxid as an analgesic and anesthetic agent in obstetrics. P. F. W.

THE COLLECTED PAPERS OF THE MAYO CLINIC, ROCHESTER, MINN. Edited by MRS. M. H. MELLISH. Vol. XI, 1919. Pp. 1331; 490 illustrations. Philadelphia and London: W. B. Saunders Company, 1920.

VOLUME XI of the Collected Papers of the Mayo Clinic brings together the published work of fifty-four members of the staff for the year 1919 in an imposing volume of 1331 pages. The present volume follows the same physical make-up as its predecessors and contains many well executed illustrations. The one hundred and eleven papers composing the text are somewhat loosly grouped in nine sections, Alimentary Canal; Urogenital Organs; Heart; Blood; Skin and Syphilis; Head, Trunk and Extremities; Nerves; Technic and General Topics.

While the initial volume of this series was almost entirely of a surgical nature, the expansion and development of departments of correlated branches of medicine in this clinic with their consequent literary output, has given the volumes of recent years, and especially the present one, an extremely broad outlook. So one finds papers ranging from "Studies on the Electrocardiogram," "The Etiology of Poliomyelitis," "The Relation of Mouth Conditions to General Health" on through other branches of medicine with papers of a surgical nature composing the greater part of the text. Under the section on Technic one finds not only the "Technic of Gall-bladder Exposure" but also such a purely laboratory article as "The Use of Turpentine Resin in Turpentine as a Foam Breaker."

The splendid work of E. C. Kendall, Chief of the Section on Biochemistry of the Clinic, on thyroxin appears in three papers comprising about one hundred pages. Dr. William J. Mayo contributes five papers, and Dr. Charles H. Mayo, six papers, on surgical and general topics. Under the section on general topics the activities of the pathologic and laboratory services of the A. E. F. are described by Dr. L. B. Wilson, who played no small part in bringing these services to their high degree of efficiency. The volume closes with the addresses delivered at a memorial meeting in honor of Sir William Osler. P. F. W.

THE SYMPATHETIC NERVOUS SYSTEM IN DISEASE. By W. LANGDON BROWN, M.A., M.D., F.R.C.P., Physician in Charge of Out-patients, St. Bartholomew's Hospital. Pp. 161, 9 illustrations. London: Henry Frowde, Oxford University Press, and Hodder & Stoughton, 1920.

THIS is an amplification of the Croonian Lectures for 1918 given by the author before the Royal College of Physicians of London. Originally appearing in part in the *Lancet*, they well deserve this presentation in expanded form. The book opens with a short but excellent account of the sympathetic and parasympathetic portions of the autonomic nervous system. In this the author has succeeded in giving a simple exposition by describing only the main points and by making many allusions to function. In Chapter II is treated, from a modern point of view, the pathologic physiology of the adrenals, thyroid and pituitary—all endocrine glands stimulated by the sympathetic system. Then follows the consideration of the influence of the sympathetic system and endocrine organs on glycosuria. As part of this there is a discussion of Allen's theory of diabetes, pituitary and other glycosurias and the polyglandular hypothesis. In the chapter on the sympathetic system and diseases of digestion are treated such topics as reflex dyspepsia,

enteralgia and hyperchlorhydria. Equally interesting are the discussions of the circulatory system and of vagotonia. From a consideration of the variety of subjects treated it will easily be seen what an important part the autonomic system plays in the life-processes of the individual, both in health and in disease; and the book gives an excellent presentation of the modern advances of our knowledge in this field. W. H. F. A.

Diathermy in Medical and Surgical Practice. By Claude Saberton, M.D., Hon. Radiologist to the Harrowgate Infirmary and to the Royal Bath Hospital, Harrowgate; late Hon. Medical Officer to the *X*-ray and Electric Department, Royal Victoria and West Hants Hospital. Pp. 138; 33 illustrations. New York: Paul B. Hober, 1920.

Part I of this book is devoted to technic and deals with the production of high-frequency currents, diathermy apparatus, physical properties and physiologic effects of diathermic currents and methods of application. In this part of the book a lot of valuable information is condensed in a small space and set forth in such manner that it may be easily grasped by the student.

Part II is devoted to medical applications of diathermy. These applications cover a wide range of diseases, and one cannot help but think that the author is just a bit extravagant in his claims of almost universally good results in some of the nervous conditions and affections of the thorax.

A discussion of diathermy in surgery constitutes the third and best part of this little volume, the chapter on treatment of bladder tumors being especially good. J. D. Z.

Backwaters of Lethe (Some Anesthetic Notions). By G. A. H. Barton, M.D., Anesthetist to the Hampstead General and Royal National Orthopedic Hospitals. Pp. 151; 11 illustrations. New York: Paul B. Hoeber, 1920.

In a series of seven essays Doctor Barton offers the crystallized results of his twenty years' experience in anesthesia. The essays deal in an entirely unconventional and very personal style with the various anesthetic agents used, and detail the small practical points which he has found of value. He describes anesthesia as an art, developed since the former days when "chloroform killed some on the table, but ether killed more afterward in bed." The essay on

the use and abuse of alkaloids in anesthesia should be of interest to surgeons as well as anesthetists, while the closing essay "Shoals and Rapids" narrates his experiences with some of the more common dangers in anesthesia. P. F. W.

A Manual of Pathology. By Guthrie McConnell, M.D., Pathologist to the Cleveland City Hospital. Fourth edition. Pp. 611. Philadelphia: W. B. Saunders Company, 1920.

A great deal of information is contained in this excellent little book. The author has displayed unusual ability in choosing the more important facts and presenting them clearly, briefly and accurately.

The text is divided into two parts: the first part embraces general pathology including postmortem technic, some laboratory technic and bacteriological methods and the second part covers special pathology. These subjects are arranged in the usual manner and the book should continue to prove quite useful not only for general reading and to those who wish to review the essentials of these subjects as in preparation for examinations, but as a handy laboratory manual. J. A. K.

Occupational Affections of the Skin. By R. Prosser White, M.D. (Edin.), M.R.C.S. (Lond.), Life Vice-President, Dermatologist, Senior Physician and Enthetic Officer, Royal Albert Edward Infirmary, Wigan; Vice-President, Association Factory Surgeons; Life Fellow, London Dermatologists' Society; Member, Manchester Medical and Dermatologists' Societies; Hon. Life Member, St. John Ambulance Association; Associate Editor, *Journal of Industrial Hygiene*, S.M.O. and Cadet Colonel, Church Lads' Brigade. Second edition. Pp. 360; 23 illustrations. New York: Paul B. Hoeber, 1920.

The second edition of this excellent book, inaugurated by Dr. R. Prosser White, has been entirely rewritten, and has doubled in size. This increase has, undoubtedly, been necessitated by the new trades and many combinations of chemicals which are now in use, including the eruptions which were directly caused, and some of which have appeared, as an aftermath of the war. A comparison of the first and the present second edition show the enhanced value of the latter. The volume now contains eleven chapters, with the following titles: A circumspection; a conspectus; physical agents; acids, alkalies and some metallic salts; the dermatoconioses; industries; occupations; trades; synthetic dyes; dermatitis

venenata; zoetic dermopathy. As a reference work it should be interesting to any one to read the present work carefully, as it will help tremendously in diagnosis, prevention and treatment. A considerable number of new photographs have been added, which also increase the value of the work. The references are many and will prove useful to those investigators desiring to write along these lines. F. C. K.

THE ENDOCRINES. By SAMUEL WYLLIS BANDLER, M.D., F.A.C.S., Professor of Gynecology in the New York Post-Graduate School and Hospital. Pp. 486. Philadelphia and London: W. B. Saunders Company, 1920.

"THE influence and action of the endocrine glands are evidenced by somatic, mental and psychic changes." This constitutes the premises upon which the author proceeds to explain many symptoms and disturbances that are apparent to all practitioners in medicine, unexplained by definite physical and laboratory analysis.

Beginning at birth he develops the individual physically and mentally, the completeness and efficiency of the same depending on the harmony of the pluriglandular system; discussing at length, gynecologically, from puberty to the climacterium, including the disturbance of sterility, pregnancy, labor and placental glands.

He discusses each individual gland, hyper- or hypofunctionating—pineal, thymus, parathyroid, hypophysis, adrenals, ovaries, testis, including the mammary and placental gland. He quotes freely from authoritative research, blending logically acknowledged endocrine physical defects, thereby concluding that instinct, emotions, nervous defects, mental deficiency and criminality, neuroses, psychosis and phobia can be explained by faulty balance between the endocrines.

The anamnesis and symptoms are covered in detail, concluding with several clinics and numerous cases; practical from a standpoint of diagnosis, including the glandular therapy and results.

Gynecologically and neurologically the subject is practically and exhaustively treated equally advantageous to the general practitioner and the specialist.

The cardiocirculatory changes encountered in endocrine disorders might have been allotted more space likewise so lightly has he dealt with differential diagnosis, namely, thyrotoxicosis *versus* chronic pulmonary infection, etc.

A difficult subject masterfully handled, supported by the attitude, "I give you what I have found of value." J. A. S.

REPORT OF THE SURGEON-GENERAL OF THE U. S. ARMY TO THE SECRETARY OF WAR, 1920.

THIS report is the annual report covering the general activities of the medical department for the fiscal year ending June, 1920, and containing the statistics for the United States Army for the calendar year ending December 31, 1919.

Additional factors in this report compared to the previous years are statistics concerned with the demobilization of the war army and the restoration of the sick and injured and finally aiding in the building up of the new army and the recruiting of the medical department thereof and the medical department sections of the officers' reserve corps. E. L. E.

SURGICAL CLINICS OF CHICAGO. Vol. IV, No. VI (December, 1920). Index number. Pp. 219; 57 illustrations, with complete index to Vol. IV. Philadelphia and London: W. B. Saunders Company.

THIS December number completes Vol. IV of the *Clinics*. It contains a very complete and satisfactory index to the volume, which volume has 1336 pages and 398 illustrations. This number contains nineteen separate articles by as many authors, all of whom are familiar to readers of the *Clinics*. It maintains the high standard set by the previous numbers.

From this date the *Clinics* cease to exist as the *Surgical Clinics of Chicago*, but don a new cloak and become the *Surgical Clinics of North America*. A distinctly attractive feature of this new and broader work is the plan to have each number, published every two months, devoted exclusively to the work at one great surgical center. The Philadelphia number appears in February, 1921.

E. L. E.

OPERATIVE SURGERY. By PROF. DR. VICTOR SCHMUDEN, Univ. of Halle, and ARTHUR TURNBULL, M.B., PH.B. (GLASGOW). Second edition. Pp. 350; 436 illustrations. New York: William Wood & Co., 1920.

THIS is a handbook for practitioners and students and has been remodelled to fit the latest ideas of what an operative surgery should be. Ligations which, in the past, were the important branch of surgery, have been relegated to a secondary position and more important operations are given precedence.

Only topographical anatomy and surgical technic are considered in these pages and the latter only so far as can be practised on the dead subject. The purpose of the book is to sum up and illustrate operative surgery for the beginner as well as the graduate. The book is made concise by omission of discussion of the various methods as to frequency, etc. Simple methods have been everywhere preferred to complicated ones and modern technic and the newer operations have supplanted those of time-honored usage.

The book is a good one of its kind, but, of course, is not a text-book of operative procedure in the living body. E. L. E.

PHYSIOLOGIC PRINCIPLES IN TREATMENT. By W. LANGDON BROWN, M.A., M.D. (CANTAB.), F.R.C.P., Physician with Charge of Out-patients, St. Bartholomew's Hospital; Physician to the Metropolitan Hospital, etc. Fourth Edition. Pp. 426. New York: William Wood & Co., 1920.

WE had the pleasure of reviewing the third edition of this work in 1914. Much has been learned during the intervening years concerning many points in physiology, and this much has been well woven into the fabric of the earlier edition to make this latest one even a better book than its predecessor. The same plan of subject treatment is carried out and the chapter headings remain unchanged. Brown calls well for his material upon the rich field which the English physiologic school supplies. We failed, however, to read something of Kendall's thyroxin and other interesting Cisatlantic contributions in recent years.

The chapters on diabetes and acid intoxications have received much revision. They are especially interesting because they call attention to the work of Graham, in St. Bartholomew's, on the fasting method of treating diabetes. Apparently quite independently Allen in this country, Graham in England, arrived at much the same conclusions concerning this therapeutic procedure. The war, however, prevented the publication of Graham's results in any sort of comprehensive form. Graham seems to advocate a short mitigated fast of forty-eight hours with a much more speedy addition of protein than Allen advises. Brown has had less experience with the Allen treatment, but feels that starvation to a glycosuria-free point may be more injurious to health than in the Graham forty-eight-hour method.

The chapter on irregular action of the heart remains untouched. The portion devoted to "the athletic heart" has, however, been abandoned for some lines on "the soldiers' heart" in the light of wartime experiences.

We like the book very much. It is helpful to the man who cares to apply newer physiologic principles to his clinical work. Brown has for a decade or more combined the practice of medicine in London with the teaching of physiology. The result has been the production of a splendid work with, of course, a decidedly English atmosphere. T. G. S.

THE DETERMINATION OF HYDROGEN IONS. First Edition. By W. MANSFIELD CLARK, M.A., PH.D., Chemist, Research Laboratories of the Dairy Division, United States Department of Agriculture. Baltimore: Williams & Wilkins Company, 1920.

THE limitations of this book are contained in the title. It is a detailed exposition of the colorimetric and electrometric methods for determining hydrogen ion concentration and does not enter into a discussion of the relation of hydrogen ion concentration to biological and chemical processes. The first chapter contains a general mathematical discussion of the relation of acids and bases to hydrogen ion concentration. The pH scale, buffer action, and effect of dilution are elucidated. In the course of the next sixty pages the theory and procedure in applying the colorimetric method are discussed. A brief exposition of the theory of indicators is given and in addition to directions for preparing the buffer mixtures with which the author's name is associated those for the mixtures of Sörensen, Walpole and Palitsch are also given. The electrometric method (potentiometer method) is discussed to the extent of 106 pages. In addition to an adequate presentation of the mechanical features the theoretical aspects are reviewed with considerable clarity. While the superiority of the potentiometer method over the older compensation procedures is unquestioned, in view of the expense of the apparatus it would seem as though some mention might have been made of the simpler equipment which served Sörensen and others so well.

A bibliography of sixty pages concludes the book. The references are classified and one may find what work has been done in a particular field with great facility. Among the subjects in the classification are bacteriology, blood, catalysis, cerebrospinal fluid, comparative and general physiology, digestion, hemolysis, iso-electric points, serology and urine.

The book is written from a critical viewpoint so that one may get a good idea of the sources of error and deficiencies of the methods as well as some comprehension of the direction research is taking in the elucidation of the obscure though minor phases of the general subject. R. L. S.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Lymphosarcoma, Lymphatic Leukemia, Leukosarcoma, Hodgkin's Disease.—WEBSTER (*Johns Hopkins Hosp. Bull.*, 1920, No. 358, xxxi, 458) calls attention to the confusion existing among pathologists as to the proper classification of these conditions. After the careful study of 123 cases falling into this group, all of which came to autopsy, he arrives at the following conclusions: "(1) It seems probable that lymphosarcoma, lymphatic leukemia and leukosarcoma are different manifestations of the same disease. (2) The term 'lymphadenosis, leukemic or aleukemic' would express this idea, and simplify the classification, until a definite etiological agent is found. (3) This disease is not a neoplasm, but a direct response on the part of the lymphocytes to a chemotactic influence exerted by the disease-causing agent. The presence of this substance in any tissue or organ produces there a local accumulation of lymphoid cells. (4) Diagnosis and prognosis of this disease in its early stage is difficult from the microscopical examination of a single gland because of its resemblance to certain types of benign lymphadenitis. (5) Evidence of ameboid activity on the part of the lymphocytes is indicative of a rapid, fatal course. (6) Hodgkin's disease, a distinct entity, may be diagnosed and accurately prognosed from the microscopic examination of a single gland."

Tuberculosis of the Spine Resembling Pyelitis.—FOSTER (*Jour. of Urol.*, 1920, No. 6, iv, 559) notes that occasionally disease of the spine, sufficient in extent to cause nerve injury with its resulting pain, does not cause impaired motility, and thus leads to a mistaken diagnosis. A case is reported in which the patient gave a history of unilateral pain suggesting pyelitis. Intermittent fever and pyuria were

present. Cystoscopic examination revealed pus coming from the kidney on the side of the pain. Examination of spine and radiograms negative. The diagnosis of pyelitis was made. Two months later kyphosis and signs of tuberculous disease of the vertebræ developed.

Dangers to Life Associated with Gall-stone Disease and Their Prevention.—TILTON (*New York Med. Jour.*, 1921, No. 1, cxiii, 4) considers the following as the chief dangers that threaten life: (1) Acute suppurative or gangrenous cholecystitis; (2) cholangitis; (3) malignant disease of the gall-bladder; (4) operation in delayed cases. Acute cholecystitis produces exquisite right hypochondriac pain, frequently radiating to the right shoulder. There is at times a chill. Hyperpyrexia occurs; sometimes vomiting. Examination reveals marked abdominal rigidity, and a mass caused by the distended gall-bladder and adherent omentum. Jaundice is usually absent. There is a leukocytosis with high polymorphonuclear count. The treatment advised in the severe cases is surgical, simple drainage being the operation of choice. Cholangitis implies common duct blockage with resulting infection. Jaundice is the most characteristic symptom and is often accompanied by chills, intermittent fever, sweats and prostration. The ultimate treatment is surgical. The choice of the time for operation is a question of surgical judgment. Operation is more hazardous at the height of the attack, yet if the symptoms persist for forty-eight hours and the patient's general condition is growing worse it offers the best chance for recovery. Simple drainage meets the vital indications. If the patient recovers from an attack under medical treatment he should not be allowed to run the risk of a recurrence. "One attack of jaundice associated with stones indicates operation in the absence of other factors that may contra-indicate operations in general." Malignancy of the gall-bladder is not a rare complication of gall-stones. Every chronic, thickened gall-bladder with stones has the possibility of malignant change, and should be removed. The history is that of repeated gall-stone attacks. When hepatic metastases are present the case is hopeless. Surgery may be successful if the growth is confined to the gall-bladder. Under the heading of the dangers of operation in the delayed cases, the author discusses the cases of gall-stone carriers from the standpoint of operative risk, noting the frequency with which one meets in them evidences of cardiac and renal disease. Attention is called to the fact that these delayed operations are usually more difficult and prolonged. These dangers can be avoided by operating in the early stages of the disease. The conclusion is reached that early operation in cholelithiasis is strongly indicated.

The Pulse-rate in Relation to Metabolism and Diagnosis.—(*Jour. Am. Med. Assn.*, 1921, lxxvi, 181). The fundamental work of Benedict and Murchhauser on the relationship between metabolism and pulse-rate in normal individuals is cited, as is the more recent work of Means and Aub, and Sturgis and Tompkins. The writer notes that discrepancies between pulse-rate and metabolism occur, but calls attention to the fact (Sturgis and Tompkins) that a pulse-rate at complete rest of below 90 a minute is seldom, and below 80 a minute is rarely associated with an increase in metabolism. This finding is of

much clinical importance in the recognition of the large group of nervous patients with symptoms suggesting hyperthyroidism, and in many instances of tachycardia not dependent upon thyroid disease.

Leukanemia.—SYMMERS (*Jour. Am. Med. Assn.*, 1921, lxxvi, 156) reports a case which clinically fell under this group-name, as originally described by Leube in 1900. The disorder is characterized by findings suggestive of both a primary anemia and myeloid leukemia, and is a rapidly progressive fatal malady. Stating that among hematologists the consensus of opinion is that the myeloblast is capable of differentiation into erythroblast on the one hand, and into granular leukocytes on the other, Symmers notes that in leukanemia the provocative agent seems to strike the bone-marrow with such intensity as to cause the appearance of both types of cells (erythroblastic and leukocytic) in the circulating blood. He summarizes as follows: "(1) Leukanemia is characterized clinically by an extremely rapid course and by changes in the blood, bone-marrow, spleen, liver and lymph nodes that partake both of the nature of pernicious anemia and myeloid leukemia, the causative agent acting on the hematogenic centers of the bone-marrow in such fashion as to produce marked numerical increase in those primitive cells which represent the precursors of both the erythroblasts and the granular leukocytes. The primitive cells in question are myeloblasts, as is shown by their morphology, and by the fact that they respond to the oxydase test. (2) Histogenetically, pernicious anemia, myelogenous leukemia and leukanemia are closely related conditions, and represent different quantitative responses on the part of the bone-marrow to regenerative stimuli acting on the same metrocyte, namely, the myeloblast. (3) Leukanemia is probably not an independent disease but one of a group of rapidly progressive derangements of the blood-forming tissues, due to infection."

Use of a High Fat Diet in the Treatment of Diabetes Mellitus.—NEWBURGH and MARSH (*Arch. Int. Med.*, 1920, xxvi, 647) report their studies of the use of high fat diet in the treatment of diabetes mellitus. Their observations are made on 73 cases of true diabetes mellitus. the majority of which were of the severest type. Despite this fact, they had succeeded in rendering and keeping their patients sugar-free up to the time of discharge from the hospital. The authors summarize their observations as follows: "Patients with severe diabetes, as a class, do not remain sugar-free on the usual high protein diet unless the total energy intake is kept so low that incapacity from starvation results. The only satisfactory diet is one which will keep the diabetic sugar-free, which will prevent the occurrence of serious acidosis, which will maintain nitrogen balance and which will make it possible for him to resume the ordinary activities of life. With these four points in mind, we studied the effect of a high fat, low protein, low carbohydrate diet in the treatment of diabetes. Our experience with this type of diet in the management of 73 cases has convinced us that it is capable of fulfilling these four specifications." The authors append examples of their diet.

SURGERY

UNDER THE CHARGE OF

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ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Surgical Treatment of Gastric and Duodenal Ulcer.—MAYO (*British Med. Jour.*, July 24, 1920, p. 103). If it is true that the majority of the causes of duodenal and gastric ulcer have an average duration of a number of years, many extending from twenty to thirty years, it is probable that there is an exaggerated idea of their danger to life. Few persons die from perforation, and few from hemorrhage—more, however, than die from surgical procedure. It is true that they suffer, are disabled, and should be relieved; and it is also probable that but a small percentage of the total number of ulcers are recognized or treated for the true condition. Gastric ulcers may give greater discomfort than duodenal ulcers, and, because of the danger of malignant degeneration, should be destroyed at the time of the operation unless this procedure would add unwarranted immediate risk, I believe patients who suffer from gastric ulcer should be told of this danger. In fact, the surgical treatment of ulcer is the best recognition of the value of medical treatment by permanently overcoming delay or obstruction and lowering the acidity with the patient's own alkalis.

Crucial Ligaments of the Knee-joint.—GROVES (*British Jour. of Surg.*, April, 1920) describes his operations for the repair of ruptured crucial ligaments of the knee-joint designed to restore their most important functions—namely, the checking of forward displacement of the tibia by the anterior, and of backward displacement by the posterior, ligament. The leg is encased in sterile stockingette through which a large U-shaped incision is made in front of the knee, its lowest part being just below the tubercle of the tibia, the inner limb running along the line of the inner hamstrings, and the outer one fingerbreadth on the outer side of the patella, the incision in the stockingette being fastened with clips to the skin edges. The tubercle of the tibia is chiselled off, the patella turned upward, and the interior of the joint exposed. In repairing the anterior ligament a strip of the iliotibial band, 8 inches long by 1½ inches wide, is separated, retaining its original attachment to the head of the tibia. The external condyle is drilled, so that the inner end of the hole is far back in order that the new ligament may be as oblique as possible. The front of the tibia is then drilled, so that the inner end of the hole lies just in front of the tibial spine, its external orifice being over the most prominent part of the inner tuberosity of the tibia, the proximal ends of each canal being bevelled to make smooth funnel-shaped openings. With a strip of gauze as pilot the strip of iliotibial band is pulled taut through the femur and through

the head of the tibia, and, with the knee flexed, it is fixed by sutures and one ivory nail on the inner aspect of the internal condyle. After suturing the joint capsule the tubercle of the tibia is replaced and fixed by two bone or ivory nails. A similar procedure is adopted for repair of the posterior ligament with proximal strips from the semitendinosus and gracilis tendons. These are thrust through the inner part of the posterior ligament of the knee and pulled forward until their free ends hang out from the front of the joint, and they are then passed through a hole bored through the internal condyle opening as far forward as possible on the inner aspect of the intercondylar notch. After being pulled tight, with the knee fully extended, the free ends are turned downward and attached to the inner tuberosity of the tibia, and the joint closed. The knee is put up on a back splint, with daily massage and faradism to the quadriceps after three weeks. Six weeks after the operation a light plaster case is applied and patient allowed to walk, and a moulded case with lateral hinges is used later for three to six months.

Rib Grafting Operations for the Repair of Bone Defects and Their End-results.—Eloesser (*Arch. of Surg.*, 1920, i, 428) says the rib graft is a feasible procedure. The viability of the grafts is great, even in the presence of suppuration. They are more liable to survive in the presence of infection than more massive grafts. They are rapidly absorbed. They hypertrophy slowly. They are prone to refracture (7 out of 22 cases). They are not so good as tibial grafts for the repair of large defects or when the graft is to be put under strain. They are particularly useful when no great demands are made on the strength of the bone, in repairing defects of the skull and in facial plastics. In such cases they should be used by preference. Of a series of 22 cases, 3 were failures, 13 were successes and 6 were partial successes.

The Relation of the Islets of Langerhans to Diabetes, with Special Reference to Cases of Pancreatic Lithiasis.—Barron (*Surg., Gynec. and Obst.*, 1920, xxxi, 437) says pancreatic lithiasis is a very rare disease, which occurs mostly in males during the fourth decade. The obstruction of the pancreatic duct leads to an advanced atrophy of the pancreas accompanied more or less by fibrosis. The islets may remain intact even when the acini disappear completely. The islets are epithelial structures which are entirely independent of the acini and have no relation to or communication with the ducts. Changes in the islets, such as degeneration, necrosis and fibrosis—generally occur late in the disease, probably as a result of a superimposed secondary infection, consequent to a prolonged stasis in the ducts. In complete accord with the results obtained experimentally in animals, occlusion of the ducts by calculi in man does not result in diabetes mellitus unless there be actual injury to the islets. Cases of pancreatic lithiasis presenting symptoms of hyperglycemia and glycosuria reveal definite lesions of the islets at autopsy. The present study bears out the conclusions that the islets secrete a hormone directly into the lymph or blood streams (internal secretion), which has a controlling power over carbohydrate metabolism. Attempts at regeneration of injured pancreatic tissue

manifest themselves in a definite hyperplasia of the ducts. The principal clinical findings in cases of pancreatic lithiasis are colic-like epigastric pains often associated with temporary glycosuria, steatorrhea, alimentary glycosuria, incomplete digestion of meat fibers as revealed by the persistence of the nuclei in muscle fibers in the feces, and, occasionally, the presence of whitish or grayish pancreatic stones in the feces; the late stages are often accompanied by diabetes mellitus. Operations on the pancreatic duct are often successful. The danger of fat necrosis as a result of the escape of pancreatic fluid appears to be negligible.

Jaundice and its Surgical Significance.—Mayo (*Surg., Gynec. and Obstet.*, 1920, xxx, 545) says that jaundice as a symptom of disease may present a very serious problem in tracing its cause. Fifty per cent. of cases are due to common duct obstruction by a stone and 20 per cent. are due to infective or catarrhal jaundice without duct obstruction. Most of the latter cases occur in children and young persons. From 5 to 8 per cent. of cases of jaundice are due to serious infection of the gall-bladder, possibly gangrene, with or without stones. They are usually accompanied by a degree of pancreatitis. Fifteen per cent. of the cases seen are due to cancer, one-half of these from cancer of the liver, the other half from cancer of the pancreas or the gall-bladder and ducts. A short-circuiting operation relieves the patient often for months. The author has not had a permanent cure from transduodenal extirpation of the tumor of the ampulla. In 8 per cent. of the cases the jaundice was associated with ascites in cirrhosis. In cases of late operation for chronic jaundice the "white bile" which is found at operation and the failure of the power of biliary excretion to appear within a day or two following the operative drainage is a most unfavorable symptom. Long-continued jaundice shows the coagulation time is delayed and this may become serious. The best measure to decrease the coagulation time is the transfusion of acceptable human blood. This can be repeated just before and even after operation if necessary. If the gall-bladder shows marked evidence of disease it is removed. In the more serious infection, with degrees of gangrene, the procedure depends upon the condition of the patient. Another cause of jaundice is injury to the hepatic or common ducts at operation. Jaundice in which the head of the pancreas is enlarged and hard demands most careful consideration. This may be due to pancreatitis or carcinoma. The pancreas is involved secondarily to gall-bladder disease more frequently than was supposed. The gall-bladder may usually be looked upon as the primary focus and should be removed. The cases of obstruction associated with distention of the gall-bladder are best treated by attacking the gall-bladder after it has been emptied to the duodenum. In the cases of damage to the common duct following operation the ends should be sought and anastomosed, or if impossible the upper end is anastomosed to the duodenum or prepyloric region of the stomach. The passing of the bile into the stomach causes no distressing symptoms. In 1916, 1917 or 1918 anastomosis was done in 13 cases, 2 of which died. In 2460 cholecystectomies the mortality was 1.8 per cent. Of 337 cases in which cholecystectomy and choledochotomy were both done the mortality was 3.2 per cent.

THERAPEUTICS

UNDER THE CHARGE OF

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Treatment of Congenital Syphilis.—FORDYCE and ROSEN (*Jour. Am. Med. Assn.*, 1920, No. 21, vol. lxxv) report excellent results in congenital syphilis by the use of the following treatment: Mercuric chloride, gr. $\frac{1}{10}$ to $\frac{1}{8}$, in palmitin, intramuscularly with special needle (illustrated), and neoarsphenamin, gr. 0.075 to 0.2 in 3 to 5 c.c. of water, intramuscularly. This is given once a week for six to eight weeks followed by a rest period of from four to six weeks.

Etiology of Graves's Disease.—HOOVER (*Ohio State Med. Jour.*, October, 1920) states that the suspected etiology of Graves's disease rests on fanciful speculation and that there is no rational basis for specific treatment. The only evidence incriminating the thyroid is the improvement following irradiation and the superiority of this treatment over rest is so doubtful that judgment must be suspended. While hypothyroidism is definitely proved, hyper- and dysthyroidism are not. The histology and the combination of myxedema with Graves's signs cannot be adjusted to the theory of hyperthyroidism. Frequently cases are seen with the onset of Graves's disease accompanied by diminution in size of the thyroid. These are usually rapidly fatal. Thrills and murmurs over the gland are not diagnostic of activity. They may be due to pressure of the gland or bulbous enlargement, anemia, or dilated thyroid vessels. The hyperplased gland may exhaust itself and become necrotic or fibroid. This can be prevented by iodine, and Hoover advises as protective treatment the administration of 2 grains of potassium iodide or dessicated thyroid daily. When there is an increase in the symptoms following administration of thyroid, the product should be changed as this increase is due to some unknown ptomain. Graves's disease is always accompanied by globular enlargement of the heart. There is no decrease in the volume output. Stasis is never seen in early cases, no matter how rapid the pulse. In late cases, accompanied by hypothyroidism, myocardial and renal disease stasis may appear. The cardiac enlargement requires no treatment. The diagnosis of Graves's disease should be made apart from the basal metabolism, which should be used as an index of progress. The size of the heart and the pulse-rate are more accurate guides. Regarding treatment, Hoover advises rest, *x*-ray (though the value of this is *sub judice*) and states "I am unable to see any justification for the amputation of part of the thyroid gland as a direct treatment for Graves's disease."

PEDIATRICS

UNDER THE CHARGE OF
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Studies of the Heart in Nutritional Disturbances in Infancy.—McCULLOCH (*Am. Jour. Dis. Children*, December, 1920) studied a group of sixteen infants who showed moderate or severe degrees of athrepsia. Electrocardiograms were made on admission and at subsequent times when the evidence of a material change in the clinical condition was noted. In two of these infants alteration of cardiac mechanism was noted. This alteration was a delay in auriculoventricular conduction, and changes in the form of the Q R S complex. As an explanation of these disturbances the writer offers the suggestion that they were the result of alterations in the blood and body tissues in these infants. It is probable that the changes which had taken place in the blood resulted in a deficient supply of oxygen to the heart, with incomplete or delayed removal of metabolic products from the cardiac tissues. When improvement took place in the babies the alteration in cardiac mechanism disappeared. No evidence indicating heart failure was noted.

The Influence of Water-Soluble Vitamines on the Nutrition of Dogs.—KARR (*Proc. Soc. Exper. Biol. and Med.*, January, 1920) says that studies on a few species of animals have indicated that the water-soluble vitamine is of importance to nutrition during all stages of life and that prolonged absence of it from the diet will lead to a diseased condition. In his studies he has considered the role of the water-soluble vitamine in the nutrition of the dog. The animals were fed a diet devoid of water-soluble vitamine, consisting of lard, sucrose, inorganic salts and protein in the form of casein or wheat gluten. It furnished about 70 to 80 calories per kilogram of body weight. Such food mixtures were consumed readily by the dogs during a period of from three to nine weeks. After this time they refuse part or all of their food. Characteristic symptoms were developed by some. The ultimate failure to eat was always noted. Ingestion of as little as one gram of brewers' yeast, which had been previously dried, caused a quick recovery of the desire to eat. Five grams of the dried yeast will bring about the disappearance of the polyneuritic symptoms in eight to twelve hours and a quick recovery of the animal to its normal condition. The utilization of the protein nitrogen was not affected by the lack of water-soluble vitamine. The fat-soluble vitamine is of less importance than the water-soluble vitamine in the nutrition of dogs.

Fordyce's Disease as Pseudo-Koplik Spots and a Cause of Mistakes in the Diagnosis of Measles.—REGAN (*Am. Jour. Dis. Children*, June, 1920) defines Fordyce's disease as a chronic condition of the mucous membrane of the mouth and lips which is characterized by the presence of grayish or yellowish, scanty or abundant, discrete, aggravated and often coalescent milium-like bodies, occurring more especially on the

inside of the mouth laterally along the lines of the teeth as far back as the last molar. They occur somewhat less frequently on the vermilion or mucous membrane surface of the lips. It is among the conditions of the mouth, which may simulate Koplik's spots. They are especially to be mistaken for Koplik'e spots when they exist in patients who develop German measles. The similarity of the clinical symptoms of the two diseases is further increased by the presence of the pseudo-Koplik spots. The resemblance between the two types of lesions may be rendered closer still because of the changes which the buccal mucosa undergoes in German measles which give it a deeper discoloration than normal. Fordyce's disease is quite frequently mistaken for early Koplik's spots in patients ill with various contagious diseases and exposed to measles, whose buccal mucosa is being examined daily for the appearance of Koplik's spots. The possibility of these pseudo-Koplik spots leading to errors in diagnosis when they are present in patients with suspicious-looking maculopapular eruptions from serum or antitoxin should be remembered. Well-marked and pronounced examples of Fordyce's disease are unusual in young children. Slightly marked cases are frequently seen in infancy, but the lesions are so small and often so situated so far back in the buccal mucous membrane, and is of so nearly the same color as the normal mucosa of the child, that it may be overlooked except where a careful search is being made for Koplik's spots.

Problem of Boarding-out, with an Attempted Solution. —CHAPIN (*Med. Rec.*, April, 24, 1920) has developed what is known as the Speedwell system. This has been on trial since 1902. Boarding-out is so systematized and regulated that the good points of this phase of the care of children has its best effects. This has been accomplished by developing what is known as a unit system of intensive boarding-out. A unit is a neighborhood that has been selected after a survey has been made to learn the general conditions of healthfulness and the number of good homes that may be available in the neighborhood. There is then inaugurated a constant oversight, especially as to diet and hygiene on the part of a salaried physician and nurse who are thoroughly familiar with the class of cases and competent to deal with them. The children are kept indefinitely until digestion and assimilation have improved sufficiently to result in a permanent increase in weight and strength. The work is continued during the whole year. In each neighborhood foster mothers are trained and they become fairly expert in the work. In comparing the results with institutional care to boarding-out it is found that both mortality and morbidity are less in the latter plan.

Measles: Brain Complications.—SKOOG (*Jour. Am. Med. Assn.*, June 19, 1920) reports two cases. He says that the literature indicates that the brain complications and sequelæ of measles occur much more frequently in children than in adults, and also occur much oftener during the convalescence than during the febrile or exanthem stage. He groups the brain complications and sequelæ under three headings: (1) The first group includes a certain small number of cases in which the relationship of the measles is merely incidental. The onset of the brain symptoms may be several weeks to several months after measles.

In such cases the bearing of the measles infection to the sequela may be questioned. (2) The second group includes the secondary infections due to various organisms. The bacteria may be delivered to the central nervous system by the blood stream. The mode of invasion in most instances is undoubtedly through the cribiform plate from the nasopharyngeal cavities. A great many more cases of meningitis follow measles, compared to all of the other complicating disorders of the central nervous system. (3) The third group is a less certain one, owing to the fact that the exact etiology of measles is as yet undetermined. Clinical studies of the disease lead us to believe that the blood stream is teeming with the virus. Accordingly the vascular channels of the meninges and the brain may readily become involved Some of the brain complications first manifested during the eruptive stage, or the early convalescent period may be caused directly by the virus of measles.

Transfer of So-called Normal Antibodies.—REYMANN (*Jour. Immunol.*, May, 1920), by examining the transmission of agglutinins, normally occurring in the blood, from mother to offspring in goats, has been able to prove in only one case of fourteen examined that these agglutinins recurred. In all the other cases the kids were born without agglutinins, and probably derived it from the mother through the milk, in which it is found accumulated at parturition. From the milk as well as from the kids' serum it disappears in the course of a few days, and then follows a period of a few months in which the blood of the kid is free from agglutinins. After this it reappears, probably from immunization from the flora of the digestive tract. This study was made for coli and typhoid agglutinins, and also for the agglutinins against rabbit and horse-blood corpuscles. In the blood of the kid there was found in some cases more and in others less of the so-called normal antibodies than in the blood of the mothers. Only in one case did the blood of the kid contain more than the colostrum, so that it was not possible to deduce any quantitative rule. It was found that in the colostrum the titer was higher than the serum of the mother. It was shown in one case by nursing experiments that the agglutinins are probably transmitted to the kid through the mother's milk. In another case the result was questionable. The agglutinin maximum of the blood of the kid may occur as early as about eleven hours after birth. By the injections of horse-blood corpuscles into kids it was possible to increase the agglutinating power as well against these corpuscles as against the colon bacillus, and, on the other hand, injection of the colon bacillus increased the agglutinating power against horse blood corpuscles.

Relation of Acquired Food Dislikes of Children to Diseases of Middle Life.—RICE (*Jour. Am. Med. Assn.*, July 10, 1920) says that almost without exception the adults and children possess the red blood and vigor of health are those who eat a variety of foods. They may eat irregularly and consume a great deal of what is called trash, but their appetites for the essential foods remain unimpaired. A healthy individual rarely dislikes eggs, milk, fresh meats or green vegetables. The latter type of food is the most common element in the diet of healthy individuals. A diet without green vegetables and milk is deficient. If

fresh meats are also eliminated serious metabolic disturbances will ensue. It is during the second year of life that children previously healthy on a well-balanced diet become desirous of foods that are seen and which may prove deleterious on account of habit formation even if not in themselves harmful. Discipline is necessary for the future welfare of the child. A large number of sufferers from the diseases of middle life suffer from food dislikes dating back to childhood. Rickets, scurvy, pellagra and beri-beri are due to deficient diets. The author believes that hypertension, chronic Bright's disease, visceral ptosis, gastric and duodenal ulcer and other conditions are the remote graver manifestations of improper diet.

OBSTETRICS

UNDER THE CHARGE OF

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Labor Complicated by Gangrenous Appendicitis.—GRATTAN (*Surg. Gynec. and Obst.*, November, 1919) reports the case of a primipara who had always been healthy and who had been well during the first of her pregnancy. Presentation and position were normal, but when first seen the analysis of the urine was negative. The pregnancy proceeded in a strikingly normal and healthful way. When at term the patient's physician was called by telephone to suggest something to relieve pain in the epigastrium which had started earlier in the evening and increased toward midnight. There was slight nausea, but no distinct pain anywhere. Alkalis and carminatives gave no relief. Gastric lavage and enema were given later and the patient was better throughout the day and evening. The temperature then rose slightly until it reached 101°. There were no labor pains and no distinct abdominal pain. On the next morning the temperature was 100.4°, and for the first time tenderness could be made out in the right iliac and lumbar regions and in lesser degree in the left iliac region. The point of greatest tenderness was high and external to McBurney's point, but this might result from an upward displacement of the intestines by a full-term uterus, and a diagnosis of acute appendicitis was made. The patient began to complain of labor pains, and on examination it was found that the cervix was beginning to dilate. Operation was decided upon and the abdomen was opened by a high and extremely lateral incision. When the peritoneum was opened there was a gush of several ounces of turbid fluid. A tense, fluctuating and sausage-shaped mass was found upward and behind the displaced cecum. This mass was very carefully drawn down into the wound, where it proved to be a completely gangrenous appendix, distended with fluid, but as yet without perforation. The appendix was ligated at its base with catgut and the remainder amputated. Two rubber drains were inserted and the abdomen was closed. The appendix

was firm in shape, dull on the peritoneal surface, the coats thinned by distention and the lumen contained about 2 drams of foul sanguineous pus. The muscular coats of the appendix were in a state of dissolution. There was considerable pressure on the walls of the distended organ. At its proximal end there was a coprolith. There was no omentum adjacent to the appendix. A half-hour after the operation labor began and the patient was given moderate doses of morphin. When the head reached the pelvic floor the patient complained of pain in the wound and chloroform was again given and the head carefully delivered under partial narcosis with forceps. There was no tear requiring suture. The placenta was delivered normally and the uterus contracted well without hemorrhage. The baby's pulse was good and regular, but at first it did not breathe. Oxygen and the lung motor were employed and after thirty-five minutes of intermittent use of this appliance breathing became established and the baby cried loudly. There were no marks of the forceps and no paralysis of the face or extremities. The child weighed eight pounds one ounce. Two and a half hours after delivery the patient had cyanosis and apnea, while the action of the heart continued to be regular. The baby seemed well and breathed and cried. A little later another attack occurred which required one hour and five minutes of artificial respiration, when the child seemed to be doing well. A fourth attack of apnea developed later, heart action failed and the baby died. The infant was catheterized and the urine examined for traces of morphin, thinking that perhaps the three doses administered to the mother might have affected the child. No evidence of the drug was found by toxicologic examination. As the child lived seven and a half hours after delivery, and seemed perfectly normal between the attacks of apnea, with no evidence of paralysis, the forceps could scarcely be considered the cause of its death. The most reasonable explanation of the infant's death was that of toxemia derived from the mother as the result of the appendicitis. A postmortem examination of the child was declined. There was slight nausea and inability to void urine, and fluids were taken in small quantities and the secretion of urine was normal. Later the patient vomited a large amount of mucus and bile-stained fluid. On the following morning there was irregularity of the pulse, although there was no symptom of internal bleeding. The pulse became irregular and rapid. The effort was made to introduce saline fluid and free stimulation was employed. The secretion of urine became more scanty and a large quantity of albumin appeared. Evidently the mother was profoundly toxic and had a toxic myocarditis. The wound did well. The pelvic drainage was removed but symptoms of cardiac failure developed. In spite of stimulation the action of the heart gradually failed, the secretion of urine varied, but slowly increased. On the sixteenth day after the operation the patient had considerable fever, the wound was reopened and a boggy, sanguineous exudate was found on the outer side of the wound. This was broken up and a rubber tube inserted. After this the temperature dropped to normal and the patient made an uninterrupted recovery. The last vaginal examination showed the uterus normal and that there was no residual pelvic exudate, which was unusual under the conditions. The patient finally made a complete recovery. The writer lays considerable stress on the concealed and insidious nature of the appendicitis. In the reviewer's experience this hidden development of infection of the appendix is not uncommon

during pregnancy. In one case a multipara passed through a spontaneous labor, nursed her child, made an apparent recovery and went to her home. Shortly after she was taken with symptoms of infection of the appendix and at operation the infection had attacked not only the the appendix but the right Fallopian tube. The appendix was gangrenous and the peritoneum in the right lower abdomen had become infected. With free drainage the patient recovered.

Twenty-four Breech Presentations.—Remy (*Rev. mens. de gynec. obst., et de pediat.*, 1919, 125) reports 17 breech presentations which occurred in his own experience. The delivery was spontaneous in 13 of these. In 4 some obstetric operation was necessary, in 3 for insufficiency of expulsive force and once for the posterorotation of the child's back as well as rotation of the head. In all of the 17 cases a living child was delivered, and most of them breathed well. The writer believes that when uterine contractions are good and the breech and body of the child are born early the obstetrician should lower the arms, which is easily done, and use classical and ordinary methods to secure the expulsion of the head. It is not correct to apply the term dystocia to such cases. These, however, are the most favorable type. In 7 other cases of breech presentation extraction of the child was necessary because of complications. In two the child was dead before anything could be done. In two others (primipara) the child died during delivery. In both of these cases the greater part of the child's body was above the pelvic brim. Of the total number of 11 cases reported in which intervention was absolutely necessary eclampsia was present in 4. In the eclamptic cases a living child was delivered. Because of the complications of breech labor the writer urges that whenever possible the head be substituted for the breech before measures to deliver the patient are undertaken.

Cesarean Section from the Dead and Dying.—Linzenmeier (*Med. Klin.*, 1920, Nr. 17, p. 439), in four operations upon dead or dying mothers, succeeded in delivering three children alive. In view of the importance of prompt operation, he believes that the operator should not wait until the actual moment of dissolution in the mother. Death is preceded by a period of unconsciousness and this would be the favorable time for operation. In fact, so soon as it is seen that death is approaching, in the interest of the child, the operation should be performed. Acute pulmonary tuberculosis is one of the conditions frequently justifying the operation. Where the patient has rapidly advancing tuberculosis, pregnancy should be interrupted so soon as possible. If, however, the case is not seen until the second half of pregnancy, delay may be practised in the hope of obtaining a living child. In these cases, the operator should not wait until the operation is done as a last resort. With patients where the conditions are all favorable for a rapid and easy vaginal delivery, this may be practised oftentimes including vaginal Cesarean section. If, however, the mother's condition is such that the child is already somewhat injured by the approaching maternal death, abdominal Cesarean section is demanded, because it exposes the child to the least risk and delivers it in the quickest manner possible. If the patient is not comatose, anethesia must be employed.

GYNECOLOGY

UNDER THE CHARGE OF

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Periodic Headaches of Ovarian Origin.—In the fall of 1916 a married woman, aged thirty-eight years, came to ABBOTT (*New York Med. Jour.*, 1920, cxii, 724) seeking relief from headaches which she had had for many years, but had become very troublesome only in the last few months. They were coincident with the menses, beginning slightly before and lasting five to seven days. These headaches were entirely absent during pregnancy but always recurred after the termination of gestation. Abbott's attention was at once centered upon the production of the corpus luteum as the possible and probable explanation of this phenomenon. So definite and suggestive was the history that he immediately determined to try the administration of dried corpora lutea. Five grains of a standard product was given three times a day and the patient was instructed to continue this until a perceptible result was obtained and after that to reduce the dose for the next two weeks after each period, but return to the full dose twelve to fourteen days prior to the period. After three months the patient returned, reporting that the headache occurring with the first menses after beginning treatment was not so severe as usual. The second one was but slight, and there was no headache at all with the third period. The patient did not come again for five or six months. At this third visit she reported that she had stopped the medicine entirely after the third month of treatment and that she had no headache for about three months more, when a recurrence took place and the medicine was resumed. For a few times she took the medicine before each period and has had no headaches since the first recurrence. Over two years from the beginning of treatment the patient reported that she had taken no capsules for a year and had had no menstrual headaches. Since treating this patient Abbott has treated about 25 women with headaches of this type and the results have been highly gratifying. With the majority of patients, however, it seems to be necessary to repeat monthly a brief course of corpora lutea prior to each menstrual period. The treatment has never provoked an increased flow or any other untoward symptoms. In order to obtain definite results the cases must be carefully selected, discarding all that do not fall under the definite symptomatology and course outlined. This type of headache always occurs, in the first place, with some definite time relation to the menses. It may be during the period only. It may begin a few hours or even a week

before the period. In some cases it always comes after the close of the menstrual flow. The headaches never occur during pregnancy. This feature has been absolutely uniform in those women who have born children or who have had children since the inception of this type of headache. A third feature of these headaches is that they become worse as the patient approaches the menopause and reach their maximum with the usual height of the nervous symptoms of this period of life. Periodic headaches of ovarian origin cease after the full completion of the ovarian atrophy of the climacteric. The cessation of such headaches will therefore occur after the operative removal of the ovaries for any cause whatsoever and will be very materially hastened by proper dosage of *x*-ray or radium. When very severe, this type of headache is usually accompanied by nausea and vomiting and for this reason women often speak of them as sick headaches. Care should be observed that this does not lead to confusion with other forms of headache associated with nausea or vomiting, or both.

Exstrophy of the Bladder in the Female.—In looking up the literature on exstrophy of the bladder, BURKE (*Ann. Surg.*, 1921, lxxiii, 100) was unable to find a single instance of operative cure of such a condition in a female subject by the extraperitoneal method and, therefore, presents the detail of a case of this congenital anomaly in a female which he has succeeded in curing. The technic which he followed in this case began with the introduction of catheters in the ureters for about six inches. This served a twofold purpose, (*a*) as guides, giving definite knowledge of the position and course of the ureters, and (*b*) as conductors of urine from the ureters, rendering the operation field free of contamination. Beginning at the mucocutaneous border of the bladder, he made a two and a half inch incision through the skin and fat in the median line, down to the rectus fascia and the fascia was split the whole length of this incision. Beginning at the posterior wall of the bladder at the lower end of the incision, with gauze on the index finger, separation of the bladder from the peritoneum was accomplished with little difficulty. The bladder was then completely freed from the abdominal wall and the gauze dissection was continued down to the ureters, which were easily distinguished on account of the catheters previously inserted. After freeing the bladder and isolating the ureters for about one and a half inches, the bladder was split in the middle line down through the trigone. Beginning at this point he incised circularly the bladder about a quarter of an inch away from the ureter meatus, therefore making a button or rosette of bladder with the meatus in the center. In this manner the blood supply as well as the sphincter action of the ureter outlet was preserved. Then two mattress sutures of catgut were inserted into each rosette, leaving the ends long. At this stage of the operation it was necessary for an assistant to dilate the anal sphincter and introduce the index finger into the vagina and the middle finger into the rectum. A long forceps was passed up into the rectum, the middle finger of the assistant acting as a guide, and pushed up to meet the operator's finger from above. Between the operator's finger and the assistant's middle finger were rectal wall and pelvic fascia. A small incision was made over the tip of the forceps and the latter pushed up through

the rectum to grasp the long ends of catgut attached to the bladder rosette containing the ureter opening. The catgut with the ureter was then drawn through the opening made in the rectum and at the completion of the operation the ureters hung suspended for about three-quarters of an inch in the rectum, about one inch above the anal sphincter. In transplanting these lower ends of the ureters it was attempted to prevent any kinking. The remaining part of the bladder was extirpated and iodoform gauze was packed loosely down to the rectum on either side of the vagina, to act, first, to stop the oozing which was considerable, and second, to help prevent the ureters from slipping from the rectum. The abdominal wound was closed in the usual manner down almost to the pubes, just enough opening left to permit the two gauze strips to emerge. The catgut strands hanging in the rectum, attached to the rosettes, were brought outside the anus and kept taut by adhesive plaster in order to prevent slipping back of the ureters from the rectum and a piece of rubber tubing was then placed in the rectum.

Operative Treatment of Bladder Neoplasms.—Although the electrical cauterization of bladder neoplasms has been successfully employed for many years by BEER (*Ann. Surg.*, 1921, lxxiii, 72) since he introduced it to the profession, he has repeatedly urged that this method of treatment should not be employed in malignant growths or in benign growths (*a*) that are not readily accessible, (*b*) that surround the sphincter and bleed so that a thorough treatment is impossible, (*c*) that are so numerous that the bladder is studded with tumors (papillomatosis), and (*d*) those cases that for one reason or another are intolerant and cannot be regularly cystoscoped. In cases of the above mentioned types, operation must be employed and the technic which has given Beer the best results is as follows: After irrigating the bladder, it is emptied so that when it is opened the wound is not flooded with fluid containing tumor cells, and the patient is placed in the Trendelenburg position and a suprapubic incision is made. The bladder is exposed and freed extraperitoneally and the urachus is doubly clamped and cut. After the bladder is well freed down to the trigone, the perivesical space is packed off with gauze pads and the bladder is incised either through its anterior, posterior or lateral wall, depending upon the position of the growth. Sponging within the bladder should be reduced to a minimum. When the growth is exposed it is immediately cauterized *in situ* with the electric cautery and every suspicious spot is treated similarly, remembering that a too extensive cauterization is preferable to a too superficial one. If the bladder wall is infiltrated, a wide cautery resection of this area is performed. If a ureter is involved in the infiltrated area it is left attached until this area is resected and is then cut away from the resected portion at a distance from the growth and is implanted into a healthy part of the bladder just before the bladder wounds are sutured. The use of clamps with teeth, such as the Kocher, which produce minute perforations in the bladder wall, thus possibly producing implants, should be avoided throughout the operation. In order to further prevent the possibility of bladder implants, the incision which opened the bladder is carefully seared with the cautery and then

the whole wound is filled for about five minutes with alcohol, the bladder being allowed to slip back into its bed so that its cavity as well as the protected gauze is exposed to the effects of the alcohol, which it is hoped will coagulate any potential cell implants that have broken away during the various manipulations. The bladder is then sponged dry and closed, after making provision for suprapubic tube drainage. In closing the bladder, a layer of plain catgut sutures is used to infold the charred edges of the incision and over this a layer of chromic gut is applied to support the first layer. The abdominal incision is closed in layers with rubber dam drainage to the bladder both above and below the tube which enters that organ.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Complement-fixation in Influenza with B. Influenzæ Antigens.—Complement-fixation tests on serums from thirty-five patients, using several strains of Bacillus influenzæ as antigens were performed by Cooke (*Jour. Infect. Dis.*, 1920, xxvii, 476). The antigens consisted of moderately opaque saline emulsions from twenty-four-hour blood agar plates, which were heated to 65° C. for one hour and titrated to determine anticomplementary qualities. Inactivated serums in quantities of 0.1, 0.05 and 0.01 c.c. were used for each fixation test. The hemolytic system consisted of two units of complement with 0.5 c.c. of a 1 per cent. suspension of sheep corpuscles, sensitized with two units of hemolysin. Twenty-one of the cases were of uncomplicated influenza and fourteen had bronchopneumonia, one of which was fatal. The blood for testing was obtained after the temperature was normal, usually in the second week after the onset of the first symptoms. In all, 162 tests were made on 24 sera of older children and adults, using 16 strains of Bacillus influenzæ and over 60 per cent. of the reactions were positive. Of 59 tests on eleven children with 8 strains of Bacillus influenzæ, only 17 were positive, 6 of these being weak reactions. The controls included 13 cases, and of the 120 tests done 16 per cent. were positive. One of the positive reactions was given by the serum of an apparently healthy carrier. No specific antigenic relationship could be detected between the 16 strains of Bacillus influenzæ with the serums tested. The author concluded that the complement-fixation test could not furnish sufficient evidence to justify the conclusion that Bacillus influenzæ is the sole etiologic agent in influenza although the results indicated that the influenza bacillus is pathogenic and infects many, if not all, patients with influenza.

Experimental Study of the Mononuclear Phagocytes of the Lung.—The importance of endothelial reactions in the bodily defense has long been urged by Mallory. Their activities in the lung were studied by Haythorn, largely from the standpoint of the disposition of inspired dust and carbon particles in anthracosis. From experimental work as well as the study of human tissues, he concluded that the dust cell was of endothelial derivation, though he could not be specific as to its point of origin. Six years after this work, Sewell reverted to the earlier theory that the dust phagocytes were derived from the respiratory epithelium. Recently, PERMAR (*Jour. Med. Res.*, 1920, xlii, 9), using intratracheal injections of particulate matter (carmine powder in suspension) combined with simultaneous and subsequent *intra vitam* staining (isamine blue) in experimental animals, has been able to demonstrate that the endothelium of the vascular bed of the lung gives rise by proliferation to wandering endothelial phagocytes, the endothelium of the blood capillaries being especially active in this regard. These wandering endothelial cells migrate directly to the air sacs, to save immediately as active phagocytes for the foreign particulate substances lying there. The endothelial phagocytes were shown to be identical with "dust cells" and could be followed from this origin in the vascular endothelium, and subsequently wandering through the interstitial tissues into the air-sacs, where they phagocyted carmine granules. Further, these cells were found in lymphatics, migrating toward the hilus, and also in the lymph nodes at the hilus. The rate of endothelial proliferation was shown to be directly dependent on character and the intensity of the irritant employed in the intratracheal injection. Phagocytosis was found to begin within one hour, and to be well established after six hours; while at the expiration of twenty-four hours practically all pigment had been taken up by the numerous free endothelial phagocytes present. The rate of migration was fairly rapid, carmine bearing mononuclears being found in the peribronchial lymph nodes within twenty-four hours. This does not continue at this rate, however. The respiratory epithelium was never found to contain pigment granules, nor did it ever show evidence of contributing to the production of mononuclear phagocytes. The mononuclear leukocytes of the circulating blood could also be ruled out, since none of the blood cells took vital stain under the condition of administration.

Intestinal Obstruction: A Study of the Influence of the Bacterial Flora on the Toxemia of Acute Obstruction.—It has been demonstrated that the material which collects in the intestine above the point of obstruction is toxic and that the absorption of this material is responsible for the toxemia of acute obstruction. That the toxic materials in intestinal contents both under normal conditions and in cases of acute obstruction may arise independently of food and in the absence of gastric juice, pancreatic juice and bile has been shown, as has the fact that the secretions of the normal intestinal mucosa are not toxic when absorbed from the peritoneal cavity. It seems probable that the principal toxic factor in the contents of the obstructed intestine belongs to the group of poisonous substances which are produced by the action of bacteria on proteins or their split products. CANNON, DRAGSTEDT and DRAGSTEDT (*Jour. Infect. Dis.*, 1920, xxvii, 139) studied the rela-

tionship of the intestinal flora to the toxemia resulting from complete obstruction induced by occluding the distal end of the cecum in white rats. Before and after operation, the intestinal flora was controlled by diet. It was found that, at death, proteolytic floras supplanted aciduric ones, in spite of the diets fed. The average period of survival was longer in the rats previously fed with bread, milk and lactose than those fed on meat. The authors conclude that it is not possible to prevent the onset of toxemia in acute intestinal obstruction by feeding diets which in normal animals bring about an aciduric intestinal flora, but they believe the onset of toxemia may be delayed in proportion to the degree that the aciduric flora may be maintained, presumably developing simultaneously with the appearance of a proteolytic flora.

Bacillus Perfringens: Toxin and Antitoxin Production.—Although the urgency for an antiserum against gas gangrene has largely subsided with the cessation of war, a sufficient number of cases are encountered in civil practice to warrant further work for practical and scientific purposes. CAULFEILD (*Jour. Infect. Dis.*, 1920, xxvii, 151) has recorded certain observations made in the production and standardization of an antiserum to Bacillus perfringens and a combined antiserum to Bacillus perfringens and Bacillus tetani. Fresh muscle glucose broth, as advised by Bull and Pritchett, was adopted in the preparation of toxin. Utmost care was necessary to maintain virulence and every attempt to raise the virulence by direct animal or bird (pigeon) passage failed, while virulence could be increased by cultural methods. By injection of pigeons with short incubation cultures, it was found that even six to eight hours' incubation produced a culture of high virulence. To avoid loss of toxicity during filtration the time involved was shortened by passing the oil-covered cultures through paper mash and then through a medium Berkefeld candle into colored glass bottles containing a few c.c. of sterile paraffine oil. The antiserum was standardized by neutralization as shown by absence of reaction at the site of inoculation into the pigeon breast muscles. Two M.L.D's of toxin were used as the test dose and the smallest amount of serum which would allow the bird to survive thirty-six hours was determined. The serum toxin mixture was incubated for one hour and the smallest amount of serum required to save the life of the bird estimated as one antitoxin unit. The most effective antiserum was the monovalent which protected against two M.L.D's of the toxin in a dilution of 1 : 200. No practical difference was noted between deaths due to whole cultures and toxins. The interval between the time of inoculation and death in the pigeon was rapidly shortened by comparatively slight increase in the dose. The sera of two horses immunized against Bacillus perfringens developed a titer of from 1 : 600 to 1 : 800. By concentration methods it was found that the horses treated with Bacillus perfringens developed as many as 40,000 antitoxin units per c.c., while those receiving both Bacillus perfringens and Bacillus tetani developed up to 15,000 for the former and up to 700 for the latter.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Production in Monkeys of an Acute Respiratory Disease Resembling Influenza by Inoculation with Bacillus Influenzæ.—BLAKE and CECIL (*Jour. Exper. Med.*, December, 1920, No. 6, xxxii, 692) state that Bacillus influenzæ can initiate in normal monkeys an acute infection of the upper respiratory tract which may be complicated by acute sinusitis, tracheobronchitis, hemorrhagic edema of the lungs, bronchiolitis, and bronchopneumonia. This disease appears to be essentially identical with influenza with respect to its clinical course, symptoms, and complications. The etiologic relation of Bacillus influenzæ to acute sinusitis, tracheobronchitis, bronchiolitis, and bronchopneumonia is established. Although it seems reasonable to infer from the results of the experiments that Bacillus influenza is the specific cause of influenza, a definite conclusion is not permissible, since it is impossible to determine whether the respiratory disease produced in monkeys with Bacillus influenzæ is identical with influenza or merely similar to it. The experiments are advanced, therefore, as evidence in favor of the etiologic relation of Bacillus influenzæ to influenza.

Studies on Experimental Pneumonia. (X) Pathology of Experimental Influenza and of Bacillus Influenzæ Pneumonia in Monkeys.—CECIL and BLAKE (*Jour. Exper. Med.*, December 1, 1920, No. 6, xxxii, 719) found that virulent influenza bacilli, when injected into the nose and throat of monkeys (*Cebus capucinus* and *Macacus syrichtus*), excite an acute inflammation of the upper respiratory tract, characterized by swelling and hyperemia of the mucous membrane, infiltration of the mucosa and submucosa with leukocytes, desquamation of epithelial cells, and the production of a mucopurulent exudate. The accessory sinuses are often implicated in the infection. Experimental Bacillus influenzæ infections of the upper respiratory tract are frequently accompanied or followed by bronchiolitis, peribronchial infiltration, and bronchopneumonia with hemorrhage and edema in the early stage, emphysema and bronchiectasis in the later stages. In general, the process closely resembles uncomplicated Bacillus influenzæ pneumonia in man. The injection of virulent influenza bacilli directly into the trachea of monkeys induces in them an experimental bronchiolitis and hemorrhagic bronchopneumonia, similar in all respects to spontaneous Bacillus influenzæ pneumonia. In experimental Bacillus influenzæ infections of either the upper or lower respiratory tract the influenza

bacillus can usually be recovered during the acute stage by culture, either pure or in association with other bacteria. In experimental Bacillus influenzæ infections in monkeys characteristic changes occur in the thymus gland—hyperplasia of the follicles, distention of the lymphatic channels, and infiltration of the parenchyma with leukocytes. This enlargement appears to be merely part of a general hyperplasia of the lymphoid structures in the cervical and thoracic regions.

Chilling of the Body Surface in Relation to Auto-infections of the Upper Respiratory Mucous Membranes.—GRANT, MUDD and GOLDMAN (*Jour. Exper. Med.*, 1920, xxxii, 87–112) report improvements in a method previously described (*Jour. Med. Research*, 1919, xl, 53–101) for detecting alterations in the blood supply of the throat by following with thermophiles, applied to the mucous membrane and skin, local temperature changes. The palatine tonsils, like the palate, pharynx and skin, react to chilling of the body surface with reflex vasoconstriction and ischemia. On rewarming the subject the tonsils tend quickly to recover their blood supply, in some instances actually becoming hyperemic; the skin returns to about its control condition; the palate and pharynx remain somewhat ischemic. The hypothesis is advanced that one factor in the beneficial hardening effect of cold bathing and outdoor living, with its incident heightened resistance to respiratory infection, may be the training of the vasomotor system in the direction of development in the pharynx of a reaction of hyperemia following chilling, similar to that observed in certain instances in the tonsils of the present subjects. The flora of the pharynx and tonsils, studied with daily swabs, showed in several instances, after experimentation, changes apparently due to proliferation of one of the microörganisms already present. In one case Streptococcus hemolyticus, in one Micrococcus catarrhalis, and in a third Bacillus influenzæ was the organism showing a relative increase in numbers. The first two instances were associated with sore-throat, the third with slight constitutional symptoms. Because of trauma and other factors it is by no means clear that these bacterial changes had anything to do with the chilling. However, it seems at least likely that the mucous membrane ischemia resulting from prolonged or excessive chilling might so lower local resistance as to permit of auto-infection. The fact is emphasized that *excessive* exposure only is warned against. Good ventilation and circulating air in buildings, cold weather and out-of-door living are needed for vigorous health; many people are unquestionably benefited by cold bathing. It is also emphasized that colds dependent primarily upon contagion from outside sources are probably of more frequent and widespread occurrence than auto-infections.

Some Possibilities in the Statistical Analysis of Case Reports of Venereal Diseases.—PIERCE and SYDENSTRICKER (*Public Health Reports*, August 27, 1920, No. 35, xxxv, 2046), in a preliminary statistical study, present data indicating that (1) the highest incidence of venereal diseases occurs at nineteen years for females and about two years later for males; (2) the highest incidence is earlier among negroes than among whites; (3) gonococcus infections in both males and females occur earlier in life than does syphilis.

Children's Teeth, a Community Responsibility.—CLARK and BUTLER (*Public Health Reports*, November 19, 1920, No. 47, XXXV, 2763) in their introduction dwell on the prevalence of decayed teeth and the necessity for prophylactic measures. In addition to bacteria, the following are given as actual and potential *causes of dental decay:* (1) Low resistance of the teeth to decay because of developmental defect (antenatal and postnatal). (2) Faulty diet, both of the mother during pregnancy and of the child. (3) Neglect of dental attention through ignorance of parents. (4) The cost of dental attention, a serious consideration with families of low economic status. (5) Failure of the child to call attention to the condition of the teeth, either because it is too young or because of fear. (6) Lack of dental facilities, so common in rural sections. The effects of dental decay are considered with reference to (1) growth; (2) resistance to communicable diseases; (3) preservation of facial symmetry, and (4) degenerative diseases. Mouth hygiene is discussed and the details of community prophylaxis are considered in considerable detail. The relation of dental clinics to parents and guardians, school authorities and taxpayers, is set forth. The choice of a toothbrush and the use of this article are considered in detail. Lime water is recommended as an effective mouth wash.

One or Several Species of Malaria Parasites.—MAYNE (*Public Health Reports*, November 26, 1920, No. 48, XXXV, 2846) refers first to the practical importance of classification of types of malarial fevers from the standpoint of treatment. The literature bearing on the numbers of species of malarial parasites is reviewed and the writer's own experience is presented. It is shown that in experimental transmissions the infection conveyed runs true to type, and the author expresses the opinion that plurality of species is the normal status.

Ambulatory Treatment of Drug Addiction.—The U. S. Public Health Service (*Public Health Reports*, December 3, 1920, No. 49, XXXV, 2914) reviews the administrative factors of the ambulatory treatment of drug addicts. It is pointed out that legal opinion is expressed that this form of treatment is presumptively a violation of the Harrison Narcotic Drug Law. The order of the Commissioner of Health of Pennsylvania in prohibiting ambulatory treatment is given, as well as comments on the opening of a "clinic" in New York City, and the opinion of a Committee of the Institute of Criminal Law and Criminology.

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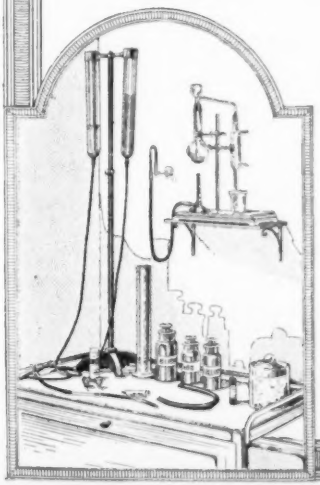

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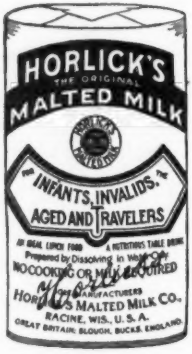

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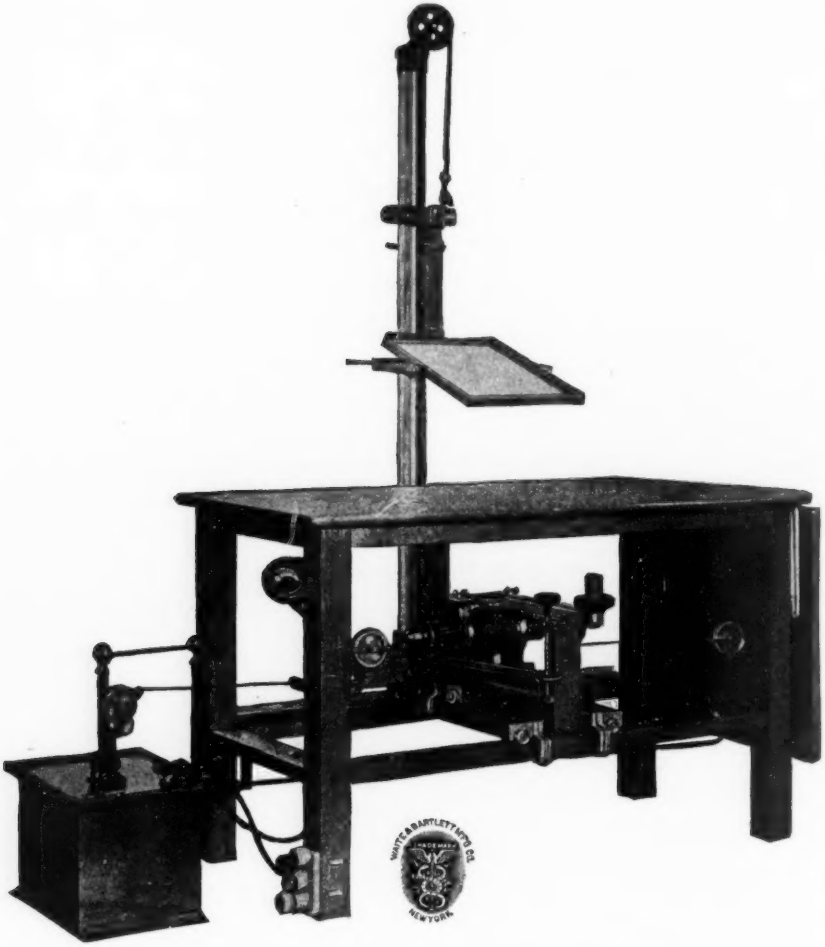

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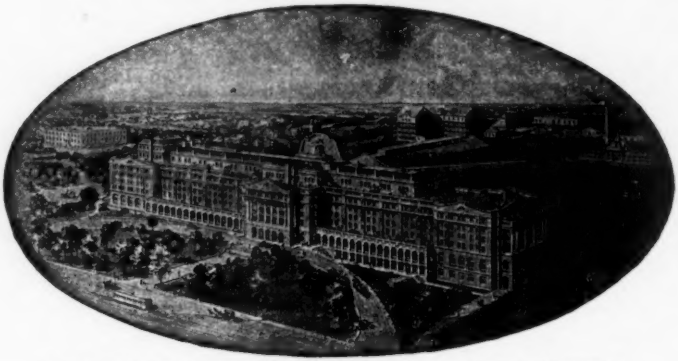

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